



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

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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

June 17, 2022

Re: Animal Welfare Assurance
A3056-01 [OLAW Case 1I]

Dr. Lance McMahon
Senior Vice President for Research
Texas Tech University Health Sciences Center - Lubbock
3601 4th Street-Mailstop 6252
Lubbock, TX 79430-6252

Dear Dr. McMahon,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your June 10, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Texas Tech University Health Sciences Center (TTUHSC), following up on an initial report on May 31, 2022 and an interim report on June 7, 2022. According to the information provided, OLAW understands that an animal activity was performed without prior approval from the Institutional Animal Care and Use Committee (IACUC). Specifically, due to confusion in the review process, mice underwent an oophorectomy procedure which had not been described in the approved protocol. Research staff were proficient in the conduct of the procedure and there were no adverse effects on the animals.

The corrective actions consisted of amending the protocol, having veterinary staff review the content of a protocol prior to training staff in a new technique, ensuring that investigators only conduct animal activities which are included in the protocol, and adjusting the institutional conflict of interest procedures.

OLAW understands that the protocol involved was not PHS-supported, but concurs that the incident was serious and supports the actions taken by the IACUC. The establishment and application of policies and practices that are consistent with the provisions of the PHS Policy at TTUHSC are commendable and avoid the perception of a double standard. We caution, however, that the use of data acquired under non-IACUC approved conditions is usually not accepted by peer-reviewed journals as the attestation cannot be made that the work was conducted in full compliance with all applicable regulations and standards. Also, had this been PHS-supported, the unapproved activity must not be charged to the grant. Thank you for keeping OLAW apprised on this matter.

Sincerely,

(b) (6)

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

cc: IACUC Chair



A3056-1I

June 10, 2022

Axel V. Wolff, MS, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare (OLAW)
National Institutes of Health
RKL 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

Confidential – Medical Committee Document

RE: Assurance # D16-00032

Dear Dr. Wolff:

Subsequent to your correspondences with IACUC Chairman, Dr. Samuel Prien, who initially reported an animal incident from our facility to you on 5/31/2022, I am writing today to provide the final report for this incident with our plan for corrective action (attached).

Dr. Prien asked that I retract the initial report that the studies involved were funded by NIH. This was in error as the studies in question were funded using local sources.

The full IACUC reviewed the subcommittee's report in today's monthly IACUC meeting and voted unanimously to accept the report and its plan of corrective actions to prevent a reoccurrence. I have reviewed their recommendations in my role as Institutional Officer for TTUHSC and believe the plan of action to be sound. Therefore, I have instructed Dr. Prien that we will adopt these corrective actions moving forward. We hope our corrective action plan meets with your approval.

Please do not hesitate to contact me if you have any concerns, and be assured TTUHSC is committed to maintaining the highest ethical standard as they involve not only animals, but all of our research efforts.

Sincerely,

(b) (6)

Lance R. McMahon, PhD
Senior Vice President for Research and Innovation

c: Samuel Prien, PhD, IACUC Chair

OFFICE OF RESEARCH

3601 4th Street – MS 8252 | Lubbock, Texas 79430 | 806.743.3600

Violations Subcommittee Hearing and Findings for the Issue Reported to OLAW 5/31/2022

Respondent:



Complainant:



This report was prepared for OLAW as required under PHS Policy IV.F.3., the *Guide*, and NOT-OD-05-034.

Executive Summary:

The purpose for this report is to notify OLAW of an incident of noncompliance as required by regulation. A procedure was performed on animals without appropriate IACUC approval. The procedure not approved was similar to a sham procedure that was approved, and was performed while training the Respondent and other research personnel by the Complainant. The internally funded unapproved procedure was then performed by the Respondent or research personnel under Respondent's supervision. The problem occurred when a conflict of interest plan required a different reviewer be assigned to review the Respondent's protocol which led to a lack of communication. After the incident was reported, OLAW was promptly notified, the Respondent submitted an Amendment to add the procedure for appropriate IACUC review, another veterinarian reviewed the study and confirmed the noncompliance, and the IACUC Violations Subcommittee met as described in the policy addressing noncompliance. To prevent a recurrence, the decision was made to add the IACUC Chair and personnel responsible for animal care be assigned as members of the full committee review team in the future for when reviewing Respondent's studies.

Initial Report to OLAW:

This is to notify OLAW of a potential protocol violation involving an NIH-funded study. It has been reported that mice were undergoing a surgical procedure that is described in the grant but which was not contained within the approved IACUC protocol. However, because of a unique oversight issue with this protocol, a conflict of interest between the Respondent and the Complainant which necessitated protocol review by the IVET of our sister institution, there may have been some confusion about what had been approved.

In brief, during our semi-annual reviews, the Complainant determined the laboratory was performing an oophorectomy procedure on mice that were not defined in the protocol. However, the Complainant has been the one to teach the lab the procedure. The Complainant reported the issue to me as Chair of the IACUC. Because of the aforementioned conflict, I asked for an independent review of the findings by an outside IVET from our sister institution, who agreed with the finding.

While both IVETs reported the violation, both feel there may have been confusion about the approved procedure or when the approval would be necessary as the IACUC and Respondent tried to manage the conflict of interest. The Respondent immediately added the procedure via amendment.

Because both IVETs agreed a violation had occurred, we will convene the Violations Subcommittee. We will focus both on the actual violation and if the management system put in place to manage the conflict might have led to confusion.

I want to stress that all involved agree that the lab was fully trained to perform the procedure and that the issue appears to be one of paperwork approval rather than risk to the animals. I also want to stress the Respondent has complied with all requests to fix issues discovered.

Because of timing issues, it is doubtful the subcommittee will have concluded its hearings and have its reports to the full IACUC before its next scheduled meeting on June 10. If not, the final report of this incident will not be available to the IO until our July meeting on July 8.

Subcommittee Meeting held 6/6/2022:

Individuals Present: Violations Subcommittee. However, as the IVET was the Complainant and part of the conflict-of-interest issue, he was replaced on the Subcommittee by the Chief Compliance Officer from the Office of Research. During the open portion of the meeting: The IACUC Administrator, a representative from the Office of General Counsel, and at varying times, the Complainant, the Respondent, and a member of the Respondent's lab. During the closed portion of the meeting, only members of the Subcommittee were present to discuss the problem, solution, and outcome.

The hearing began with the Subcommittee reviewing its role in the violations review process and a very quick overview of the issues to be addressed.

The Subcommittee then met with the Respondent. The Respondent reviewed their work and acknowledged that oophorectomy surgeries had been performed in the summer of 2021 and in the early spring of 2022. An important point of clarification that was revealed during these discussions was the funding source for the procedures in question. Paperwork indicated that these studies were paid for by both local and federal sources. However, during discussions, the Respondent stated the experimental procedures were funded using local startup funds, and no federal (NIH) funding was involved. A Subcommittee member inquired how different the oophorectomy was from the sham surgery approved in the protocol and if this was simply an extension of approved work. However, it was pointed out that the sham surgery would not involve organ removal and was therefore not covered under the approved protocol. The Respondent then pointed out that the Complainant had provided training in the oophorectomy technique and had been present at numerous procedures. The Respondent then stated they had inquired if an amendment was necessary and felt the Complainant had not insisted it was necessary at the time.

The Respondent was then excused, and their lab staff member was interviewed. The single question posed to the staff member was if the Complainant had provided training in the oophorectomy procedure in question. The staff member confirmed then Complainant provided the training. With that, the staff member was excused.

The Subcommittee then interviewed the Complainant, who acknowledged they had supplied training to the Respondent and their staff. The Complainant further acknowledged they had not confirmed the procedure had received approval before supplying the training. However, given the PI's history of seeking approval, they had assumed it had been sought and approved. The Subcommittee Chair asked if this issue might have occurred due to the review process's special arrangements to accommodate the conflict of interest between the Respondent and Complainant. They (the IVET) acknowledged this might have led to part of the issue. However, the Complainant pointed to the OLAW requirement that all procedures must be reviewed and approved, and responsibility for seeking approval was the responsibility of the Respondent as PI.

With the conclusion of the interview of the Respondent, the Complainant, IACUC Coordinator, and Legal Counsel were excused, and the subcommittee began deliberations.

Findings:

1. While there is a dispute as to why it occurred, all parties recognize that there was a protocol violation, as a surgical procedure, i.e., oophorectomy, was being performed, which was not explicitly described in the Respondent's IACUC protocol.
2. However, the procedure is within the scope of the Respondent's work, and the procedures performed are similar to approved procedures within the IACUC protocol.
3. Further, the Complainant provided the lab with training in the procedure.
4. The disconnect appears to be due to a plan put in place by the IACUC Chair to manage a conflict of interest between the Respondent and the Complainant, which had the veterinary review of the protocol done by the IVET from our sister institution. The plan addressed the immediate conflict but separated the Complainant from their normal knowledge of the protocol (because they do Vet reviews on all other protocols).
5. Finally, the subcommittee wishes it known; while the Complainant reported this issue as required, they also wrote a letter indicating they felt there was no ill-intent on the part of the Respondent and the Respondent immediately submitted an amendment.

Corrective Actions Recommended to Full Committee for Corrective Actions

1. The Respondent immediately amended the protocol to reflect what is being done to the animals (as mentioned above, the Respondent has already done so).
2. All agree there was no intent to circumvent regulatory control, and repeating these experiments would require additional animals to undergo experimental treatments. Therefore, it is recommended that the Respondent have full access to previously collected data as the procedures fit within the overall goals of the Respondent's studies.
3. Best practices moving forward should include the TTUHSC IVET reviewing protocols before supplying training to a laboratory in a new technique.
4. The Respondent will be reminded that it is ultimately their responsibility to ensure their work is fully described in protocols. Further, the Subcommittee recommends following the rule of when in doubt, it is always better to submit an amendment for review.
5. Concerning the conflict of interest:
 - a. All are reminded that working with animals in research is a privilege, and all are obligated to ensure the welfare of the animals over any other issues.
 - b. The Chair recognizes that the current attempt to manage the conflict of interest may have led to the present issue in this instance. However, the conflict of interest remains between the Respondent and Complainant; therefore, the Chair has suggested the following modification to prevent a reoccurrence of issues. This management plan aims to eliminate even the perception that protocols from the Respondent are treated any differently than all other protocols managed by TTUHSC, its representatives, or IACUC as it comes to favoritism or excessive oversight. Therefore:
 - i. Protocols from the Respondent will continue to be reviewed by the IVET of our sister institution.
 - ii. However, the TTUHSC IVET will be made aware of the review before presentation to the full committee and may make suggestions in the animals'

- i. Protocols from the Respondent will continue to be reviewed by the IVET of our sister institution.
- ii. However, the TTUHSC IVET will be made aware of the review before presentation to the full committee and may make suggestions in the animals' best interest. It is left to the discretion of the full committee to accept or reject these suggestions.
- iii. Responsibility for the primary review of these protocols will be shifted to either the IACUC Chair or Vice-Chair, and every effort will be made to ensure either the Chair or Vice-Chair will be part of the semi-annual lab inspection team to visit this laboratory to ensure protocols match work being done in the lab.
- iv. Per federal regulation, the TTUHSC IVET must and will remain responsible for the health and safety of these animals and must be free to take any actions necessary to provide immediate care they deem necessary for the welfare of animals, including euthanasia.
- v. However, they must report any instances where animals are euthanized or removed from a Respondent protocol to the IACUC Chair.
- vi. At the discretion of the IACUC Chair, the IACUC Chair may refer actions taken to an outside veterinarian for review of their appropriateness. If such action is taken, the IACUC Chair will make the IO aware of both the request and review.
- vii. The Respondent is encouraged to report any perceived oversight irregularities directly to the IACUC Chair for review and, if necessary, corrective action. Issues that go beyond IACUC authority will be referred to the IO, or the IO's named representative, for an institutional response.
- viii. This management program will remain in place for a minimum of 24 months when it will be reviewed by the IACUC Chair and the IO, or the IO's named representative, to determine its continuing necessity.

If approved by the full IACUC, both the Respondent and Complainant will be made aware of this modification to this conflict of interest management plan in writing.

IACUC Violations Subcommittee

(b) (6)

Sam Prien, PhD

June 7, 2022

Date

June 7, 2022

Date

June 8, 2022

Date

Confidential Medical Committee Information

4

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, June 15, 2022 8:58 AM
To: Prien, Samuel
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Possible Protocol Violation Assurance # D16-00032 (A3056-01)

Thank you for this report, Dr. Prien. I will send a response soon.

Axel Wolff

From: Prien, Samuel <Samuel.Prien@ttuhsc.edu>
Sent: Monday, June 13, 2022 1:06 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: McMahon, Lance <Lance.McMahon@ttuhsc.edu>; (b) (6)
(b) (6)
Subject: [EXTERNAL] RE: Possible Protocol Violation Assurance # D16-00032 (A3056-01)

Good Afternoon Dr. Wolff,

I have attached Dr. McMahon's (our new IO) letter and the final report of the suspected protocol violation first reported to you on 5/31/2022. Please let me know if anything else is required at this point.

Sincerely,

Sam Prien, Ph.D.
IACUC Chair

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Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, June 7, 2022 7:23 AM
To: Prien, Samuel
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Possible Protocol Violation Assurance # D16-00032 (A3056-01)

Thank you for this update, Dr. Prien. I will add this information to the case file.
Axel Wolff

From: Prien, Samuel <Samuel.Prien@ttuhsc.edu>
Sent: Tuesday, June 7, 2022 12:31 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: McMahon, Lance <Lance.McMahon@ttuhsc.edu>; (b) (6)
Subject: [EXTERNAL] RE: Possible Protocol Violation Assurance # D16-00032 (A3056-01)

Dr. Wolff,

I wanted to update you on the potential violation first reported to you on 5/31/2022. We held the subcommittee hearing today. One critical piece of information that was clarified during this hearing was the source of funding used. I had initially indicated the fund for these experiments were from an NIH source. However, the PI has three separate protocols. The protocol in question is funded totally from a local source (there was an accidental typo on the application due to a copy and pasting error). I apologize for this confusion.

We hope to present the subcommittee's findings to the full committee this Friday at our scheduled IACUC meeting. If we can do so, we should be able to meet with the IO and finalize our report to you in the near future (I know our IO is scheduled to be out next week).

Sincerely,

Sam Prien, Ph.D.
Professor and IACUC Chair

From: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Sent: Wednesday, June 1, 2022 6:54 AM
To: Prien, Samuel <Samuel.Prien@ttuhsc.edu>
Cc: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: RE: Possible Protocol Violation Assurance # D16-00032 (A3056-01)

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Thank you for this detailed preliminary report, Dr. Prien. We will open a new case file and look forward to receiving the final report from the IO after the IACUC has completed its investigation. In the final report, please identify the source of funding for this project.

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: Prien, Samuel <Samuel.Prien@ttuhsc.edu>
Sent: Tuesday, May 31, 2022 1:40 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6) McMahon, Lance
<Lance.McMahon@ttuhsc.edu>
Subject: [EXTERNAL] Possible Protocol Violation Assurance # D16-00032 (A3056-01)

Dr. Wolff,

This is to notify OLAW of a potential protocol violation involving an NIH-funded study. It has been reported that mice were undergoing a surgical procedure that is described in the grant but which was not contained within the approved IACUC Protocol. However, because of a unique oversight issue with this protocol, a conflict of interest between the PI and IVET which necessitated protocol review by the IVET of our sister institution, there may have been some confusion about what had been approved.

In brief, during our semi-annual reviews, our IVET determined the laboratory was performing an oophorectomy procedure on mice that were not defined in the protocol. However, the IVET has been the one to teach the lab the procedure. They reported the issue to me as chair of the IACUC. Because of the aforementioned conflict, I asked for an independent review of the findings by an outside IVET from our sister institution, who agreed with the finding.

While both IVETs reported the violation, both feel there may have been confusion about the approved procedure or when the approval would be necessary as the IACUC and PI tried to manage the conflict of interest. The PI immediately added the procedure via amendment.

Because both IVETs agree a violation has occurred, we will convene the Violations Subcommittee. We will focus both on the actual violation and if the management system put in place to manage the conflict might have led to confusion.

I want to stress that all involved agree that the lab was fully trained to perform the procedure and that the issue appears to be one of paperwork approval rather than risk to the animals. I also want to stress the PI has complied with all requests to fix issues discovered.

Because of timing issues, it is doubtful the subcommittee will have concluded its hearings and have its reports to the full IACUC before its next scheduled meeting on June 10. If not, the final report of this incident will not be available to the IO until our July meeting on July 8.

Sincerely

Sam Prien, Ph.D., HCLD, FNAI
IACUC Chair

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Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: Prien, Samuel <Samuel.Prien@ttuhsc.edu>
Sent: Tuesday, May 31, 2022 1:40 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: [REDACTED] (b) (6) McMahon, Lance
<Lance.McMahon@ttuhsc.edu>
Subject: [EXTERNAL] Possible Protocol Violation Assurance # D16-00032 (A3056-01)

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Sincerely

Sam Prien, Ph.D., HCLD, FNAI
IACUC Chair

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