



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

November 12, 2019

Re: Animal Welfare Assurance
A4730-01 [OLAW Case B]

Dr. Parwinder Grewal
Executive Vice President for Research &
New Program Development
University of Texas Rio Grande Valley
1201 West University Drive
Edinburg, TX 78539

Dear Dr. Grewal,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your November 11, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Texas Rio Grande Valley (UTRGV), following up on an initial report on August 26, 2019. According to the information provided, OLAW understands that opossums on an approved viral study infected non-study animals. Transmission may have occurred when mothers cannibalized infected offspring.

The corrective actions consisted of the following:

- Isolating all viral infected animals.
- Not approving new protocols until the health status can be established for all animals in the colony.
- Ensuring that all staff on the protocol have been appropriately trained.
- Having the investigators provide information regarding the status of a confirmative virus assay.
- Having the investigators provide updates on virus testing and colony management.
- Having staff handle cages under biosafety level two (BSL-2) procedures; labeling cages as to level of infection.
- Collecting serum and tissue from animals to assess level of colony infection.
- Retraining research staff on BSL-2 procedures.
- Continuing refresher training; having cage wash operated by trained personnel.
- Ensuring all cages are clearly marked.
- Transferring animals between protocols must be approved by the Institutional Animal Care and Use Committee (IACUC).

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November 12, 2019
OLAW Case A4730-B

- Having training include information on prevention of contamination.

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 UTRGV are commendable and avoid the perception of a double standard. 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
Robert Gibbens, D.V.M., USDA-APHIS-AC

November 11, 2019

19-20:1015

Dr. Brent Morse, D.V.M., DACLAM
Acting Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Via email to: olawdco@mail.nih.gov

Dear Dr. Morse:

The University of Texas Rio Grande Valley (UTRGV), in accordance with Assurance A-4730-01 and PHS Policy IV.F.3., provides this Final Report of serious noncompliance regarding an incident involving *Monodelphis domestica*.

Preliminary Report:

A Preliminary Report of Non-Compliance was submitted on this incident by the (b) (6) (b) (6) to the Office of Laboratory Animal Welfare via email OLAW@OD.NIH.GOV on August 26, 2019.

Explanation of Incident:

Protocol AUP-2016-005, titled "Small Animal Models of Viral Pathogenesis" was intended to investigate the pathology of Zika Virus. During the conduct of the study an inadvertent potential exposure to *Monodelphis domestica* occurred when pups at the embryonic/fetal stage of development were inoculated with ZIKV, and later, their mothers were returned to a separate animal use protocol (AUP-2015-004) for the purpose of breeding.

The exposure was self-reported by the principal investigators as a consequence of research conducted under AUP-2016-005 to the UTRGV Institutional Animal Care and Use Committee (IACUC) on August 5, 2019.

On August 6, 2019, the chair of the IACUC discussed the incident with the committee during a convened meeting. As a result, the IACUC determined two primary causes for the non-compliance:

1. Potential contamination of non-study animals through improper handling and use of potentially infected animals, and
2. Lack of understanding of *Monodelphis domestica* behavior by IACUC members and researchers that may result in transmission of Zika virus when the protocol was initially approved (such as mothers cannibalizing infected offspring).

Office of the Executive VP for Research, Graduate Studies & New Program Development

ESSBL 5.101
1201 West University Drive
Edinburg, Texas 78539
(956) 665-3883

BBRHP 2.210
One West University Blvd.
Brownsville, Texas 78520
(956) 296-1549

utrgv.edu

Short Terms Corrective Actions:

On August 7, 2019, the IACUC called for the following immediate actions:

1. Immediate isolation of all animals known to be currently infected with Zika virus, including all animals in cages marked as being in protocol AUP-2016-005, if any. These animals will not be available for research purposes.
2. No new protocols using *Monodelphis domestica* will be approved until the health status of the individuals in the animal colony can be determined.
3. The principal investigators shall ensure that all personnel listed on the respective AUPs (2015-004 and 2016-005) have been properly trained.
4. Investigators shall provide a timeline on the availability of enzyme-linked immunosorbent assay (ELISA), details of the validation of the ELISA, and the number of animals and sampling technique that will be used to test samples for the ELISA on any member of the colony.
5. Investigators shall provide weekly updates on activities completed with ELISA testing and colony management and compliance.
6. For the safety of the animals and personnel, the IACUC stressed that *all* animals and cages must be considered infected or contaminated and handled with strict adherence to ABSL-2 procedures and cages are to be handled from least to most likely to be infected. Cages shall be labeled with their level of suspected likelihood of infection for quick identification.
7. Laboratory Animal Resources shall collect serum from the colony and provide blinded samples to the investigators once the IACUC confirms that the ELISA is ready to be used. Once results are decoded, a sub-section of animals will be euthanized for tissue analysis by PCR. As the ELISA test will let us know about recent exposure, the PCR validation will let us know if there is any chance that a negative result by ELISA may still harbor the virus for potential future release. This will inform the IACUC's final decision on how the colony will be managed.
8. Refresher training on Husbandry and BSL-2 Safety shall be provided to the investigators and individuals listed on the protocols.

Long Term Corrective Actions:

1. Continued refresher husbandry training with increased over-sight by Laboratory Animal Resources. The IACUC would like to have the cage wash area strictly operated by trained Laboratory Animal Resources staff.
2. All animals must be housed in clearly marked cages as to the protocol they are on.
3. No animals shall be moved between protocols without IACUC approval.
4. Refresher training on prevention of contamination within an animal facility.

Grant/contract number: N/A

Impact on PHS-supported activities:

The work done with the opossum colony does not involve any PHS-supported activities. All funding, to-date, has been internal. The potential effect on other research in the building is the unexpected spread of ZIKV to animals housed in other rooms within the facility without a means to test or treat the animals. Based on the preliminary data, we do not feel this is likely, but none-the-less it is the concern.

Compliance with terms and conditions:

This incident does not involve PHS-supported activities.

UTRGV 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 Christopher Vitek, PhD, IACUC Chair at christopher.vitek@utrgv.edu or (b) (6)

Thank you for your consideration in this matter.

Sincerely,

(b) (6)

Parwinder S. Grewal, Ph.D.
Executive Vice President and Institutional Official

ec: Christopher Vitek, Ph.D., IACUC Chair
Cordelia Rasa, Director Laboratory Animal Resources

(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, November 12, 2019 7:42 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Final Report of Non-Compliance

Thank you for this report. We will send a response soon.

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

From: (b) (6)
Sent: Monday, November 11, 2019 2:11 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Christopher Vitek <christopher.vitek@utrgv.edu>; Cordelia Rasa <cordelia.rasa@utrgv.edu>; (b) (6)
(b) (6) Institutional Animal Care and Use Committee <iacuc@utrgv.edu>
Subject: Final Report of Non-Compliance

Dear Dr. Morse,

Please find attached the final report from a preliminary report sent to OLAW on August 26, 2019 by (b) (6) of a Non-Compliance for an incident involving short tail opossums that were contaminated with zika virus.

Please do not hesitate to contact us if anything else is needed.

Best,



(b) (6)

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Ward, Joan (NIH/OD) [E]

From: Ward, Joan (NIH/OD) [E] on behalf of Laboratory Animal Welfare, Office of (NIH/OD)
Sent: Monday, August 26, 2019 1:08 PM
To: (b) (6)
Subject: RE: Preliminary Report of Noncompliance

Thank you (b) (6) for this preliminary report. We will open a case file and await for your final report soon.

Regards,
 Joan

Joan Ward
 Program Specialist
 Office of Laboratory Animal Welfare
 National Institutes of Health
 6700B Rockledge Dr., Suite 2500
 Bethesda, MD 20892
 301-496-7163
wardjoa@od.nih.gov

From: (b) (6)
Sent: Monday, August 26, 2019 12:24 PM
To: Laboratory Animal Welfare, Office of (NIH/OD) <OLAW@OD.NIH.GOV>
Cc: Parwinder Grewal <parwinder.grewal@utrgv.edu>; (b) (6) Christopher Vitek <christopher.vitek@utrgv.edu>
Subject: Preliminary Report of Noncompliance
Importance: High

Director, Division of Compliance Oversight-

The University of Texas Rio Grande Valley (Assurance Number A4730-1) is sending a preliminary report to OLAW. The reportable situation is: ***conditions that jeopardize the health or well-being of animals.*** We will send the thorough report with the full explanation of the situation, including what happened, when and where, the species of animals involved and the category of individuals involved. Also, we will describe the steps taken by UTRGV and the corrective action plan and schedule to be carried out.

Brief Overview: This was a self-reported incident of an inadvertent potential exposure to Monodelphis Opossums occurring when pups at the embryonic/fetal stage of development were inoculated under an approved protocol with Zika Virus, and later, their mothers were returned to the breeding colony. The protocol was approved for certain Monodelphis who were not part of the colony that was exposed.

Please feel free to contact me if you have any questions prior to the thorough report. Thank you.

(b) (6)

UTRGV
 The University of Texas
 Rio Grande Valley
UTRGV.edu

(b) (6)