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

April 25, 2019

Re: Animal Welfare Assurance
A3433-01 [OLAW Case 2T]

Dr. Prasat Mohapatra
Vice Chancellor for Research
University of California, Davis
1850 Research Park Drive
Davis, California 95618

Dear Dr. Mohapatra,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 1, 2019 letter providing a summary report regarding a vaccine induced disease in the Titi monkey colony at the University of California- Davis. According to the information provided, OLAW understands that 64 Titi monkeys were vaccinated with a canine distemper/measles vaccine and 54 developed clinical signs. Symptoms included dermatitis, lameness, and conjunctivitis. Some non-vaccinated monkeys appeared to have contracted the virus and presented with a mild rash.

Actions taken in response consisted of suspending research activities, separating animals to allow easy access to food and water, hand feeding compromised animals, evaluating serology, euthanizing three compromised animals, providing analgesics and fluids as needed, and providing antibiotics to animals with pneumonia. It was determined that a different manufacturer made this lot of vaccine and used a different cell type to grow the viruses. This batch was found to be safe in infant rhesus macaques but not in the Titis. The vaccine will be further tested to evaluate which component caused the problem and the monkeys will be followed to assess seroconversion of any non-vaccinated animals.

Thank you for providing this update on a serious incident which appears to have been addressed quickly and comprehensively to prevent additional morbidity and mortality. OLAW concurs with the actions taken by the institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals.

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

A3433-21

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO • SANTA BARBARA • SANTA CRUZ

OFFICE OF RESEARCH

1850 RESEARCH PARK DRIVE
DAVIS, CALIFORNIA 95618

**PRASANT MOHAPATRA**
VICE CHANCELLOR FOR RESEARCH

TELEPHONE: 530.754.7764
RESEARCH.UCDAVIS.EDU

April 1, 2019

**AXEL WOLFF, M.S., D.V.M.**
Deputy Director
Office of Laboratory Animal Welfare
National Institutes of Health
RKL1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

**RE: Institutional Report - D16-00521 # (A3433-01)**
**Follow-up to adverse effect report for 2018 Titi clinical cases of vaccine induced disease**
**CNPRC base grant number P51OD011107**

Dear Dr. Wolf:

In accordance with Assurance D16-00521 # (A3433-01) and PHS Policy IV.F.3., UC Davis is providing a comprehensive summary report of the 2018 vaccine induced disease that occurred in our Titi monkey colony. This situation was previously reported in September 2018 and discussed with you over the phone on multiple occasions with our IACUC Director, Donna Routley. This incident was self-reported to USDA.

In August 2018 the CNPRC vaccinated 64 Titi monkeys with 0.25 ml of the Vanguard DM (canine distemper/measles) vaccine. Between 9-15 days post vaccination animals presented for lameness/polyarthritis, papular rash, and conjunctivitis. All affected animals (54) had dermatitis and of those, approximately 20 animals showed signs of lameness or reluctance to move. We collected skin biopsies that showed lesions consistent with viral infection such as morbillivirus (potentially measles or canine distemper). Three non-vaccinated animals presented with a mild rash that was consistent with the papular lesions seen on the infected animals. We suspected there was limited transmission of the vaccine virus.

A subset of animals became significantly compromised and the family groups were housed in quads to ensure easy access to food and water. The laboratory staff suspended all research activities during

the illness. The lab staff hand fed compromised animals multiple times per day to help support them. Clinical laboratory abnormalities included profoundly elevated GGT (1000-3000) in a few animals, anemia in 2 animals, and severely elevated bilirubin in one animal. Ultimately 3 animals were euthanized due to clinical compromise related to the infection. Subsequent histopathology found the most significant damage to epithelium of the bile ducts and pancreas for 2 of the cases. One of the euthanized animals had clinical evidence of abnormal clotting and had developed a secondary bacterial pneumonia. All 3 cases had changes in the skin, kidneys, and gut.

The histopathology results for the biopsies and the first necropsy were rushed to aid in the management of the other affected animals. All animals showing signs of discomfort were provided analgesics at clinical discretion (meloxicam, buprenorphine, and or Simbadol). Animals appearing dehydrated were given supportive fluid therapy as needed. Once we learned of the pathologist's suspicion of a secondary bacterial pneumonia, the clinically compromised animals were also treated with a course of antibiotics.

This lot of measles vaccine had been used without issue in rhesus macaque infants concurrently. Historically we have used the same vaccine in Titi monkeys, but it is currently produced by a different manufacturer. Investigative conversations with the manufacturer revealed that the vaccine viruses are not grown on the same cell type and we suspect this may have contributed to genetic changes - making the vaccine no longer safe for use in Titis.

We have saved a sample of the vaccine from one of the lots used in these Titis and are interested in using PCR and sequencing to confirm if this disease was caused by the attenuated measles or distemper virus. We are also planning to serologically evaluate the Titis over time to confirm if any non-vaccinated animals seroconverted.

If you have any questions, please do not hesitate to contact our IACUC Director at (b) (6) or by email at dmroutley@ucdavis.edu.

Sincerely,

(b) (6)

Prasant Mohapatra
Vice Chancellor for Research

/pk

c: IACUC
AAALAC

## Morse, Brent (NIH/OD) [E]

**From:** OLAW Division of Compliance Oversight (NIH/OD)
**Sent:** Wednesday, April 10, 2019 12:17 PM
**To:** Donna Routley; OLAW Division of Compliance Oversight (NIH/OD)
**Subject:** RE: Institutional Reports - D16-00521 # (A3433-01)

Thank you for providing these reports Ms. Routley. We will send official responses soon.

Best regards, Brent Morse

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



**From:** Donna Routley [mailto:dmroutley@ucdavis.edu]
**Sent:** Monday, April 01, 2019 6:28 PM
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
**Subject:** Institutional Reports - D16-00521 # (A3433-01)

Hello,

Please find the attached five signed reports from UC Davis, assurance D16-00521 # (A3433-01). These had previously been reported to OLAW. For the instances involving USDA covered species, each incident was self-reported to USDA. These reports have been copied to AAALAC.

Please let me know if you have any questions.

Kind regards,
Donna Routley

Donna Routley, RVT, RLATg, CPIA
Director, IACUC
Office of Research
University of California Davis
(b) (6) (office)
dmroutley@ucdavis.edu