



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

July 23, 2019

Re: Animal Welfare Assurance  
A3448-01 [OLAW Case 1A]

Bruce Doll, DDS, Ph.D., MBA  
Assistant Vice President for Technology  
Research and Innovation  
IACUC Institutional Official  
Uniformed Services University of the Health Sciences  
4301 Jones Bridge Road  
Bethesda, MD 20814

Dear Dr. Doll,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your 15 July 2019 letter reporting a noncompliance with the PHS Policy on the Humane Care and Use of Laboratory Animals at the Uniformed Services University of the Health Sciences. Your letter supplements information provided in the initial email report received on March 20, 2019. According to the information provided, OLAW understands that on 6 March 2019 eight ferrets were subjected to a blast-induced injury followed by a CHIMERA (Closed-Head Impact Model of Engineered Rotational Acceleration)-induced injury. The first animal to undergo the procedure experienced significant bleeding from the nose and ear and a much slower recovery from the injury. Veterinarians were consulted and the experiment continued with ferrets 2-7 which resulted in bleeding similar to the initial animal. The eighth animal stopped breathing when removed from the CHIMERA and attempts to revive him were unsuccessful. It was subsequently determined that a repair to the CHIMERA machine resulted in increased PSI. It was determined that four of the animals had incurred skull fractures. It was not noted if this activity was PHS-funded.

The corrective actions consisted of removing the surviving seven ferrets from any further blast or CHIMERA procedures. The CHIMERA has been recalibrated and a lower velocity has been used on a new cohort of eight ferrets with no bleeding. The IACUC also made recommendations that the CHIMERA device should be calibrated between each cohort; that the gaskets on the device should be changed regularly; that any bleeding should stop the experiment until a CT scan can be performed and that a CT scan should be included for all animals, and; if bleeding is noticed after either BLAST or CHIMERA, all experiments should be stopped and a veterinarian should be contacted.

OLAW believes that the corrective and preventive measures put in place by the Uniformed Services University of the Health Sciences are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals for institutional self-monitoring and self-reporting. As noted in previous reports, please indicate in future reports if the activity was/was not PHS or NSF-funded. OLAW appreciates being informed of this issue and finds no cause for further action.

*Page 2 – Dr. Bruce Doll*  
*July 23, 2019*  
*OLAW Case A3448-1A*

Sincerely,

(b) (6)

Brent C. Morse, DVM  
Director  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare

cc: IACUC Contact



## UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

OFFICE OF THE VICE PRESIDENT FOR RESEARCH  
4301 JONES BRIDGE ROAD  
BETHESDA, MARYLAND 20814-4799  
www.usuhs.edu



15 July 2019

Axel Wolff M.S., D.V.M.

Director, Division of Compliance Oversight Office of Laboratory Animal Welfare  
National Institutes of Health  
RKL1, Suite 360, MSC 7982  
6705 Rockledge Drive  
Bethesda MD 20892-7982

Dear Dr. Wolff,

### Final Incident Report

OLAW Assured Facility Number D16-00258 (A3448-01)

This is a final report on an incident at Uniformed Services University of the Health Sciences (USU) (OLAW Assured Facility Number D16-00258/A3448-01) that was initially reported to the Office of Laboratory Animal Welfare (OLAW) on 20 March 2019.

On the evening of 6 March 2019, 8 ferrets were subjected to a blast-induced injury followed by a CHIMERA (Closed-Head Impact Model of Engineered Rotational Acceleration)-induced injury. The first ferret to undergo the procedure experienced significant bleeding from the nose and ear after the CHIMERA injury. Lab personnel sought assistance from the vets on duty and the AV. The ferret was unconscious and a significant amount of blood was visible. In addition to the bleeding, the animal was much slower to recover from the injury than had previously been observed for other ferrets following CHIMERA exposure. The vets observed that the animal was regaining consciousness by the time of their arrival but could not determine the cause of the bleeding.

The vets told lab personnel to continue with the experiment, and provided instructions if bleeding reoccurred in subsequent animals. However, there are different recollections as to these instructions. The vets stated that they advised the lab personnel to stop the experiment if more bleeding occurred in subsequent animals, and to contact the vet on call. The lab personnel understood their instructions to contact the vet on call if symptoms with subsequent animals experienced similar or worse bleeding than the initial animal. Ferrets 2-7 did not show worse bleeding or a decremented recovery compared to the first ferret. The eighth ferret exhibited bleeding from the nose and ears and stopped breathing immediately after being removed from the CHIMERA. Attempts

to revive him by lab personnel were unsuccessful.

Dissection of the ferret by lab personnel revealed a penetrating head injury, which suggested the instrument gave a much stronger injury than was expected. At the veterinarian's recommendation, five surviving animals that had bled after the injury underwent CT scans on Thursday, March 7th, and Friday, March 8<sup>th</sup>. It was found that four ferrets had skull fractures. The fifth ferret had only slight bleeding, and it was not clear if that blood may have been a stain from the previous animal. Through follow-on testing of the CHIMERA, it was determined that a repair in the device between the first phase of the experiment and the current phase caused the PSI of the machine to increase even though the machine was set to the same velocity.

The PI reported the incident to the IACUC on 13 March and all seven surviving ferrets were pulled from any additional blast or CHIMERA procedures but have been retained for behavioral testing. The investigators have subsequently recalibrated the CHIMERA on ferrets, and they will use a lower velocity in future experiments. They have recently performed CHIMERA + Blast on a new cohort of 8 ferrets with these new parameters, and report no bleeding.

The IACUC made the following recommendations:

- 1) The CHIMERA ferret device should be calibrated with high speed videography between each experimental cohort.
- 2) The gaskets on the CHIMERA device should be changed regularly per manufacturer's recommendations.
- 3) During testing with the CHIMERA ferret device, any sign of bleeding should be cautiously interpreted as a sign of bone fracture and testing should cease until a CT scan can be performed.
- 4) A CT Scan for all animals should be added to the protocol.
- 5) If bleeding is noticed after either BLAST or CHIMERA, all experiments should immediately stop and a veterinarian should be contacted.

The first two items have been adopted by the CNRM pre-clinical core. The PI has stated they have submitted a major modification of the protocol to the IACUC to include a CT scan on each animal. PI has assured the IACUC lab personnel will stop the experiment after any sign of bleeding, conduct a CT scan and consult a veterinarian.

The IACUC now considers this incident closed.

Sincerely,

(b) (6)

Bruce Doll, DDS, Ph.D., MBA  
Assistant Vice President for Technology Research and Innovation  
IACUC Institutional Official

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

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Monday, July 15, 2019 3:02 PM  
**To:** (b) (6) OLAW Division of Compliance Oversight (NIH/OD); dha.ncr.reg-support.mbx.r2o2@mail.mil; USARMY Ft Detrick MEDCOM USAMRMC Other ACURO  
**Cc:** Bruce Doll; (b) (6)  
**Subject:** RE: Final Report - USUHS D16-00258

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

Best regards, Brent Morse

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

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**From:** (b) (6)  
**Sent:** Monday, July 15, 2019 1:58 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; dha.ncr.reg-support.mbx.r2o2@mail.mil; USARMY Ft Detrick MEDCOM USAMRMC Other ACURO <usarmy.detrack.medcom-usamrmc.other.acuro@mail.mil>  
**Cc:** Bruce Doll <bruce.doll@usuhs.edu>; (b) (6)  
**Subject:** Final Report - USUHS D16-00258

Good afternoon Dr. Wolff,

Please see the attached final report regarding an unanticipated event from March 2019.

If you require any further information, feel free to contact me.

Thank you,

(b) (6)



20 March 2019

To Brent Morse, DVM, DACLAM, OLAW

Dr. Morse,

This is an initial report of an incident relating to the Animal Care and Use program at Uniformed Services University, Bethesda MD.

The USU IACUC received information on Thursday, 14 March, from a Principal Investigator concerning an animal welfare incident with their TBI protocol involving ferrets. The PI found that 8 ferrets showed unanticipated injuries after using the CHIMERA device. The CHIMERA device was recently serviced, and while the velocity was matched to what was used prior to the servicing, it is believed that the impact was stronger than it was before the servicing.

The IACUC determined the incident should be reported and an investigation is now in progress.

A final report will be sent to OLAW when the incident has been resolved and appropriate action has been taken. Please contact us if you have any questions or concerns.

Contact person making report:

(b) (6)

A large rectangular area of the document is redacted with a solid grey box. The text "(b) (6)" is printed in the top right corner of this redacted area.



**Wolff, Axel (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Thursday, March 21, 2019 7:15 AM  
**To:** (b) (6)  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Preliminary Report - USUHS - D16-00285 (A3448-01)

Thank you for this preliminary report, (b) (6) 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.

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

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**From:** (b) (6)  
**Sent:** Wednesday, March 20, 2019 3:38 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** usarmy.detrick.medcom-usamrmc.other.acuro@mail.mil; (b) (6)  
(b) (6) dha.ncr.reg-support.mbx.r2o2@mail.mil;  
iacuc@usuhs.edu  
**Subject:** Preliminary Report - USUHS - D16-00285 (A3448-01)

Dear Dr. Morse,  
Please find the attached initial incident report regarding a TBI protocol using ferrets at Uniformed Services University. A final report will be submitted once the investigation has concluded.  
Thank you for your review.

