



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare  
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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) 480-3387

April 6, 2022

Re: Animal Welfare Assurance  
A3306-01 [OLAW Case 3I]

Dr. Terence Flotte  
Dean, Provost and Executive Deputy Chancellor  
University of Massachusetts Medical School  
55 Lake Avenue North  
Worcester, MA 01655

Dear Dr. Flotte,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 18, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Massachusetts Chan Medical School. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the University of Massachusetts Chan Medical School Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: failure to adhere to the IACUC-approved protocol and the conduct of animal-related activities without prior IACUC review and approval. The final report states the IACUC was notified of two incidents on January 4, 2022.

The first incident involved 8 pre-catheterized mice purchased from Charles River Laboratories (CRL). The vendor guidelines for catheter maintenance required changing the catheter locking solution every 7 days. However, the protocol described a change frequency of every 3-4 days (based on guidelines from another vendor) and was not amended to include the guidelines from CRL. It is stated no adverse outcomes occurred due to the modified flushing frequency, but one animal did not recover following flushing due to catheter misplacement by the vendor. In response to the incident, the Principal Investigator (PI) amended the protocol to align with guidelines from CRL and retrained laboratory personnel on adhering to the IACUC protocol.

The second incident involved 25 mice that received subcutaneous (SQ) injections of IDH1 inhibitors. The amendment to add the procedure was approved in October 2021, but a lab member initiated the studies prior to IACUC approval unbeknownst to the PI. It is stated no adverse outcomes were associated with the unapproved studies and NIH funds were not used. In response to the incident, the following corrective actions were implemented:

- Training of all laboratory members on protocol adherence and recordkeeping, occurred on January 20<sup>th</sup>. The PI and Research Compliance Specialist provided the training.
- Implementation of bi-weekly laboratory notebook checks by the PI during one-on-one meetings with all laboratory members for more robust surveillance of animal research activities.
- Implementation of a standardized mouse census stored electronically to detail treatments and experimental manipulations associated with each mouse.

- Implementation of more robust and frequent colony surveillance by the laboratory manager and a weekly report provided to the PI.
- Initiation of a post-approval monitoring audit, which began on January 20<sup>th</sup>.

The IACUC determined the corrective actions were sufficient to prevent future recurrence at the convened meeting on January 24, 2022.

It is noted that this research is supported by NIH funding. Based on its assessment of this explanation, OLAW understands that the University of Massachusetts Chan Medical School has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy.

We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

Jacquelyn

T. Tubbs -S

Digitally signed by  
Jacquelyn T. Tubbs -S  
Date: 2022.04.06  
07:37:57 -04'00'

Jacquelyn Tubbs, DVM, DACLAM  
Senior Animal Welfare Program Specialist  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare

cc: IACUC Contact



A3306-3I

Institutional Animal Care and Use Committee (IACUC)  
Office of Research  
University of Massachusetts Chan Medical School  
55 Lake Avenue North  
Worcester, MA 01655-0002

3/18/2022

Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
6700B Rockledge Drive, Suite 2500  
Bethesda, MD 20892

Dear members of the Division of Compliance Oversight,

The University of Massachusetts Chan Medical School, in accordance with Assurance #D16-00196 (A3306-01) provides this report of protocol noncompliance for your consideration, associated with IACUC protocol PROTO202100035.

On January 4, 2022, the IACUC received an anonymous report describing two incidents of protocol noncompliance:

1. 8 pre-catheterized mice were purchased from Charles River Laboratories. The catheter locking solution was changed every 7 days in accordance with the catheter maintenance guidelines established by the vendor. The IACUC protocol however, indicated a frequency of every 3-4 days. The protocol was written in accordance with Jackson Laboratories guidelines, the vendor from which the PI originally intended to purchase mice and was not amended for the change in flushing frequency. There were no adverse outcomes due to the modified flushing frequency, however, one of the 8 mice did not recover after the locking solution was changed as a result of catheter misplacement by the vendor, which was identified during necropsy. The PI has amended the IACUC protocol to align with vendor guidelines for catheter maintenance and immediately retrained laboratory personnel on adhering to IACUC protocols.
2. 25 mice received subcutaneous injections of IDH1 inhibitors (GSK864 or AGI-6780). The injections occurred on three occasions, one in late July and two in August 2021. The amendment to add the procedure was approved by the IACUC in October 2021, but a member of the laboratory initiated the studies prior to IACUC approval, unbeknownst to the PI. The mice used for these studies were produced in excess of another study and were otherwise scheduled for euthanasia. There were no adverse outcomes associated with the unapproved studies and NIH funds were not used.

The report was immediately brought to the attention of the PI who met with the IACUC Chair, Attending Veterinarian and IACUC Office Director. After evaluating records, the PI confirmed the above activities did indeed occur and implemented a series of corrective actions to prevent future noncompliance:

1. Training of all laboratory members on protocol adherence and recordkeeping, which took place on January 20<sup>th</sup>. The PI and Research Compliance Specialist provided training.
2. Implementation of biweekly laboratory notebook checks by the PI during one-on-one meetings with all laboratory members for more robust surveillance of animal research activities.



Institutional Animal Care and Use Committee (IACUC)  
Office of Research  
University of Massachusetts Chan Medical School  
55 Lake Avenue North  
Worcester, MA 01655-0002

3. Implementation of a standardized mouse census stored electronically to detail treatments and experimental manipulations associated with each mouse.
4. Implementation of more robust and frequent colony surveillance by the laboratory manager and a weekly report provided to the PI.
5. Initiation of a post-approval monitoring audit, which began on January 20<sup>th</sup>.

This report and corrective actions were evaluated during a convened meeting of the IACUC on January 24, 2022. The IACUC determined the corrective actions to be sufficient to prevent reoccurrence of noncompliant activities.

Thank you for your consideration and guidance on these matters. Please contact me with questions or concerns.

Sincerely,

 (b) (6)

Terence Flotte, M.D.  
Institutional Official  
Dean, Provost and Executive Deputy Chancellor  
University of Massachusetts Chan Medical School

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

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Friday, March 25, 2022 8:22 AM  
**To:** (b) (6)  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: OLAW Reports University of Massachusetts Chan Medical School D16-00196 (A3306-01)

Thank you for these reports. We will send responses soon.

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

**From:** (b) (6)  
**Sent:** Wednesday, March 23, 2022 2:15 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Subject:** [EXTERNAL] OLAW Reports University of Massachusetts Chan Medical School D16-00196 (A3306-01)

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Dear OLAW Division of Compliance Oversight,

On behalf of the University of Massachusetts Chan Medical School Institutional Official, Dean Flotte, I am submitting two reports for your consideration.

1. ReportOLAW\_D16-000196 (A3306-01)\_PROTO202000182
2. ReportOLAW\_D16-000196 (A3306-01)\_PROTO202100035

Please contact me with questions or concerns. We appreciate your guidance on these matters.

Thank you,

(b) (6)

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