



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) 480-3387

February 19, 2020

Re: Animal Welfare Assurance  
#A3596-01 (OLAW Case 3P)

Dr. Harry Orf  
Senior Vice President for Research  
Massachusetts General Hospital  
(b) (4) 55 Fruit Street  
Boston, MA 02114

Dear Dr. Orf,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated January 29, 2020, concerning a report of an incident of noncompliance with the Public Health Service Policy on the Humane Care and Use of Laboratory Animals within the animal care and use program at Massachusetts General Hospital. According to the information provided, OLAW understand that on October 1, 2019, two mice were found moribund and were not euthanized in a timely manner consistent with veterinary directions and were found dead the next day. OLAW also understands that two protocol components that were each separately IACUC approved, were combined, which was not IACUC approved. This work was not PHS funded.

Corrective and preventive actions included retraining on the IACUC Policy for Euthanasia, the animal study protocol (ASP), and significant changes. IACUC oversight of the ASP was also enhanced for the next three procedures.

Massachusetts General Hospital's prompt reporting of this incident was consistent with the philosophy of self-regulation. Similarly, the timely actions taken to respond to the issue were appropriate. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

(b) (6)

Catharine E. Pritchard, PhD  
Animal Welfare Policy Scientist  
Division of Policy and Education  
Office of Laboratory Animal Welfare

cc: IACUC Contact



MASSACHUSETTS  
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RESEARCH INSTITUTE

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HARVARD  
MEDICAL SCHOOL

Harry W. Orf, Ph.D.  
*Senior Vice President for Research  
Massachusetts General Hospital  
Principal Associate in Genetics  
Harvard Medical School*

January 29, 2020

Brent Morse, DVM  
Acting Director, Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
Rockledge 1, Room 3615, MSC 7982  
6705 Rockledge Drive  
Bethesda, MD 20892-7982

Subject: Serious noncompliance with PHS Policy  
Institution: The Massachusetts General Hospital  
Animal Welfare Assurance #: D16-00361 (A3596-01)

Dear Dr. Morse:

This letter is to provide you with a full explanation of the circumstances and actions taken by the Massachusetts General Hospital (MGH) Institutional Animal Care and Use Committee (IACUC) as required by Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) Section IV.F.3 following an incident that occurred. The incident was determined by the IACUC to constitute serious noncompliance with PHS Policy and is therefore reportable.

The incident involved 2 mice that were found moribund on 10/1/2019. The responsible research fellow was contacted with veterinary orders to euthanize the mice. Due to a miscommunication between the fellow and another laboratory member the mice were not euthanized and were found dead the next day. The facility veterinarian met with the fellow and remaining mice were euthanized due to poor condition. On 11/25/19, the research team met with the IACUC compliance officer and the facility veterinarian to review the incident. During the review it was determined that the procedure performed on the mice was not conducted as described on the protocol. The protocol was approved for a carbon tetrachloride-induced liver injury and fibrosis model. The protocol was also approved for a chronic ethanol-feeding experiment. The fellow combined both experiments to recreate a model of ethanol and carbon tetrachloride induced fibrosis described in the literature. This combined procedure was not prospectively reviewed and approved by the IACUC. A compliance subcommittee of the IACUC reviewed the event on December 5 and the convened IACUC reviewed the event at its monthly meeting on December 18.

The IACUC approved the following corrective actions:

- A meeting was held with the laboratory staff to discuss the incident; the requirement for the contact person to ensure that veterinary orders are followed out was emphasized.
- Additional training was required; this included training of the laboratory staff on the IACUC Policy for Euthanasia, a review of the experiments described in the approved protocol, the requirement for the protocol to be followed as written as well as the requirement for significant changes to the

- protocol to be reviewed and approved by the IACUC prior to implementation. A copy of the IACUC policy on protocol review was provided to the research team.
- For the next three procedures, the laboratory must provide documentation to the IACUC that demonstrates compliance with the approved protocol (cage side records, laboratory notebooks etc.). The IACUC compliance officer will review the documentation to ensure the corrective action plan has been implemented and is effective.

PHS/NSF funds were not implicated in this matter.

The Massachusetts General Hospital 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 me at your convenience.

Sincerely,

(b) (6)

Harry W. Orf, PhD  
Senior Vice President for Research  
Institutional Official  
The Massachusetts General Hospital

Cc: W. Zapol MD, Chair, Institutional Animal Care and Use Committee  
Cc: A. Clancy PhD, Director, Animal Welfare Assurance  
Cc: D. Jarrell DVM, Attending Veterinarian and Director, Center for Comparative Medicine

**Tubbs, Jai (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Thursday, January 30, 2020 10:27 AM  
**To:** Clancy, Anne; OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** Orf, Harry W., Ph.D.; Jarrell, Donna M.  
**Subject:** RE: Report of Serious Noncompliance with PHS Policy\_Massachusetts General Hospital\_AWA # D16-00361 (A3596-01)

Good morning,

Thank you for the report. We will send an official response soon.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM  
 Veterinary Medical Officer  
 Office of Laboratory Animal Welfare  
 National Institutes of Health

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**From:** Clancy, Anne <ACLANCY1@mgh.harvard.edu>  
**Sent:** Wednesday, January 29, 2020 4:52 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** Orf, Harry W., Ph.D. <HORF@mgh.harvard.edu>; Jarrell, Donna M. <DJARRELL@mgh.harvard.edu>  
**Subject:** Report of Serious Noncompliance with PHS Policy\_Massachusetts General Hospital\_AWA # D16-00361 (A3596-01)

Dear Dr. Morse,

Please find attached a report submitted on behalf of Dr. Harry Orf, Senior Vice President for Research and Institutional Official, The Massachusetts General Hospital, in accordance with PHS Policy IV.F.3.

Please let me know if you have any questions or require additional information.

Kind Regards,  
 Anne Clancy

Anne Clancy, PhD | Director, Animal Welfare Assurance  
 Phone: (b) (6)  
 Fax: (b) (6)  
[aclancy1@mgh.harvard.edu](mailto:aclancy1@mgh.harvard.edu)

For 24/7 assistance with critical research matters, call 617-726-HOW2 (4692)

Have an idea or a suggestion on how we can improve? Please submit a suggestion to Isuggest !

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