



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

May 12, 2020

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

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 May 6, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Massachusetts General Hospital. According to the information provided, OLAW understands that on December 2, 2019 an incident was identified wherein 60 mice had estradiol pellets surgically placed on October 2, 2019 and research agents administered on December 1, 2019. The surgical implantation of the pellets was not included in the protocol. One mouse presented with poor body condition on December 2 and was treated by a veterinarian. Four animals had been administered a research drug that was not approved and the incorrect protocol was identified on the cage-side documentation. It was stated that the animal activity was supported by the PHS.

Corrective actions included amending the protocol to add the research agent. All members of the research team were retrained in the proper use of rodent record cards and the PI has reviewed each protocol with laboratory personnel to ensure that they understand the approved models and methodologies on each protocol and the importance of following the approved protocol. The PI has reviewed institutional animal transfer processes with all members of the research team to ensure that they understand that transfers must be completed before experiments can be initiated. It is further understood that the institution will ensure that applicable costs paid from the NIH grant will be removed, and the relevant agencies will be notified.

OLAW believes that the corrective measures put in place by the Massachusetts General Hospital are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals regarding the philosophy of institutional self-assessment, self-reporting and self-regulation. We appreciate being informed of this matter and find no cause for further action by this office at this time.

Sincerely,

Brent C. Morse -S

Digitally signed by Brent C.  
Morse -S  
Date: 2020.05.12 11:32:49 -04'00'

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

cc: IACUC contact

A3596-3V



MASSACHUSETTS  
GENERAL HOSPITAL  
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**Harry W. Orf, PhD**  
Senior Vice President for Research  
Massachusetts General Hospital  
Principal Associate in Genetics  
Harvard Medical School

May 6, 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)  
NIH/NSF Grant(s): 5R01CA201500-06; 3R01CA197976-04S1

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 was identified on December 2 and involved 60 mice that were on a protocol investigating molecular pathways involved in the development of ovarian cancer. One mouse presented with mild poor body condition that was managed by the facility veterinarian. The mice had estradiol pellets implanted on October 2 and a research agent administered on December 1.

The PI and the research team met with the IACUC compliance officer and the facility veterinarian on December 13 to review the incident. The investigation determined that the estradiol pellets were implanted using a surgical method rather than the injection method approved on the protocol and four of the animals were also administered a study drug that was not described in the protocol. In addition, the incorrect protocol was identified on the cage-side documentation. A compliance subcommittee of the IACUC reviewed the event on February 6 and the convened IACUC reviewed the event at its monthly meeting on February 19. The PI took full responsibility for the incident and worked with the IACUC compliance officer to develop a corrective action plan to prevent a recurrence of this event.

The IACUC approved the following corrective actions:

- The protocol was amended to add the research agent.
- All members of the research team were retrained in the proper use of rodent record cards and other CCM cards. The rodent record card is used as a tool to ensure, and document, compliance with the treatment and monitoring plan of the approved protocol.

Brent Morse, DVM Ltr.  
May 6, 2020

- The PI has reviewed each protocol with laboratory personnel to ensure that they understand the approved models and methodologies on each protocol and the importance of following the approved protocol;
- The PI has reviewed institutional animal transfer processes with all members of the research team to ensure that they understand that transfers must be completed before experiments can be initiated.

The institution will ensure that applicable costs paid from the NIH grant will be removed, and the relevant agencies will be notified, as appropriate.

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  
cc: (b) (6)

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

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Friday, May 8, 2020 8:31 AM  
**To:** Clancy, Anne  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Report of Serious Noncompliance with PHS Policy\_Massachusetts General Hospital\_AWA # D16-00361 (A3596-01)

Thank you for this report, Dr. Clancy. We will send a response soon.  
Axel Wolff

**From:** Clancy, Anne <ACLANCY1@mgh.harvard.edu>  
**Sent:** Wednesday, May 6, 2020 10:01 AM  
**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)

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