



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

March 26, 2020

Re: Animal Welfare Assurance
A3153 [OLAW Case 2N]



The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 16, 2020 letter providing an update in response to my February 25, 2020 request regarding an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Beth Israel Deaconess Medical Center. Specifically, mice were identified with detached head-posts and the Institutional Animal Care and Use Committee was investigating whether the investigator was proficient in conducting this type of surgery. According to the information provided, OLAW understands that the surgeon was a veterinarian who had years of extensive surgical experience and had conducted numerous successful procedures. The investigator suggested that the head-post cement may have been faulty or that mishandling of the mice for injections may have weakened the posts.

The preventive actions consisted of ensuring that only trained staff will be conducting post-operative care, procedures, and injections into the implanted cannulas. The protocol was amended to describe cannula implantation and the collaboration, a different adhesive will be used, and the laboratory was placed under enhanced post-approval monitoring.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate, correct, and prevent recurrence of the noncompliance. We appreciate having been informed about this matter and find no cause for further action by this Office.

Sincerely,

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: IACUC Chair

Beth Israel Deaconess
Medical Center



HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

AB153-2N

Gyongyi Szabo, MD, PhD, FAASLD, AGAF, FACP
Mitchell T. Rabkin, M.D. Chair
Chief Academic Officer
Beth Israel Lahey Health
Beth Israel Deaconess Medical Center
Faculty Dean for Academic Affairs
Harvard Medical School

Axel V. Wolff, M.S., D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

Re: Non-compliance on Beth Israel Deaconess Medical Center (BIDMC) protocol #056-2017 titled "Role of IRFs in metabolism". This study uses mice and was funded by NIH grant # R01DK113669 under the title "TGFbeta-mediated transcriptional reprogramming of mature adipocytes in obesity".

March 16, 2020.

Dear Dr. Wolff:

On February 18th, 2020, we reported an "off-protocol" surgical procedure to OLAW, which resulted in nine cages of mice with detached head-posts that were to be used to administer agents into the brain. We provided an assessment, explanation, and a plan of action going forward in our previous letter to you. At that time, we were still gathering information regarding the lack of surgical proficiency in the collaborating lab. We have since collected this information. The researcher who performed the surgeries is a veterinarian with over 20 years of extensive experience with performing surgical procedures in animals including 5 years at BIDMC without incident. He has performed more than 50 surgeries in mice over the past year.

While the cause for the detached head-posts remains unclear, the researcher involved speculated that perhaps the cement/acrylic adhesive that was used could have been compromised or expired. He also suggested, as a possible contributing cause was that the mice were mishandled during injections post-surgery, which may have contributed to weakening of the posts.

To prevent this from happening again, the researcher will ensure that post-operative care, follow-up procedures (after surgery), and any further interventions such as injection(s) using the implanted cannulas are done properly by trained personnel. To further minimize cannula fixation

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Beth Israel Lahey Health
Beth Israel Deaconess Medical Center

issues, the researcher will now use an adhesive recommended by a neighboring laboratory with expertise in these procedures.

Additionally, the researcher who performed the surgeries will submit an amendment to the protocol that describes cannula implantation and includes the details of the collaboration between the two laboratories.

Finally, we will send our PAM Liaison to observe the next surgeries once scheduled and report any incidents immediately to the IACUC, as needed.

(b) (6)

A large rectangular area of the document has been redacted with a solid grey box.

Cc: Principal Investigators
Chief of Endocrinology
IACUC Chair
IACUC Administrator
AAALAC, International

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Beth Israel Lahey Health 
Beth Israel Deaconess Medical Center

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, March 18, 2020 6:59 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Letter to OLAW

Thank you for this report, (b) (6) We will reopen the case and send a response soon.

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

From: (b) (6)
Sent: Tuesday, March 17, 2020 4:04 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6)
Subject: Letter to OLAW

Hello,

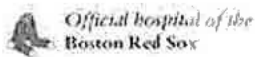
Please see the attached letter.

Thank you,

(b) (6)



Beth Israel Lahey Health 
Beth Israel Deaconess Medical Center



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6700B Rockledge Drive, Suite 2500
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Facsimile: (301) 480-3387

February 25, 2020

Re: Animal Welfare Assurance
A3153 [OLAW Case 2N]

Mr. Randall S. Mason
Vice President of Research Operations
Beth Israel Deaconess Medical Center
330 Brookline Ave., GRZ 6
Boston, MA 02215

Dear Mr. Mason,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your February 18, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Beth Israel Deaconess Medical Center, following up on an initial telephone report on February 10, 2020. According to the information provided, OLAW understands that nine cages of mice were identified with detached head-posts. The cage cards were missing, there was no information as to whether post-operative analgesia had been given, the head-post surgical procedure was not included in the protocol, and the surgery was listed on another protocol but the collaboration was not listed in either protocol.

The immediate action taken upon discovery consisted of euthanizing the mice. Both Principal Investigators were contacted and the PI responsible for the mice provided a corrective action plan. The plan stated that staff would be retrained and supervised and the protocol was amended to include the head-post surgery and the collaboration. The Institutional Animal Care and Use Committee (IACUC) is continuing to investigate whether the investigator that conducted the surgery is proficient to do so.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the IACUC to comply with the PHS Policy and requests an update by **March 23, 2020** as to the determination regarding surgical proficiency. Also, indicate whether any additional corrective actions were taken to ensure that the head-post surgery is conducted correctly and that analgesics are provided. Thank you for informing OLAW about this matter.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: IACUC Chair



Beth Israel Deaconess
Medical Center



A teaching hospital of
Harvard Medical School

Randall S. Mason
Vice President, Research
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Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
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Bethesda, MD 20892-7982

Re: Non-compliance on Beth Israel Deaconess Medical Center (BIDMC) protocol #056-2017 titled "Role of IRFs in metabolism". This study uses mice and was funded by NIH grant # R01DK113669 under the title "TGFbeta-mediated transcriptional reprogramming of mature adipocytes in obesity".

February 18, 2020,

Dear Dr. Wolff:

On January 7th, 2020, it was reported to the Attending Veterinarian by veterinary technician staff that 9 cages of mice had lost their surgically implanted head-posts. The standard cage cards indicated that the surgery was performed under protocol #056-2017, but the cages did not have surgery cards on them to indicate information including post-operative analgesia administration. The researcher listed on the cage cards and on the protocol was contacted and asked to complete an IACUC *Unexpected Outcomes Form* detailing the incident. Euthanasia of the animals was also required and humanely performed using CO₂.

The completed Outcomes report provided by the researcher noted that the surgeries performed on all of the mice were performed by a researcher in a neighboring lab. A check of protocol #056-2017, indicated that the head-post surgical procedure was not part of the approved protocol (#056-2017). Rather, approval for the surgical details were part of the other laboratory's protocol (#001-2016) and the collaboration was not part of either approved protocol.

A letter was sent to both Principal Investigator's on January 10th, 2020 requesting copies of the surgical records, explanations as to why the implants dislodged, and clarification on the reasons for the collaboration, which was not described in either protocol.

The PI of protocol #056-2017 responded detailing the events, including surgical record information and a plan to prevent this from occurring again in the future. This plan included specific details for retraining and supervising with regards to the surgical procedure, and amending the protocol to include the collaborative information and the head-post implantation surgery. This response was accepted by the IACUC at the convened meeting held on February 6th, 2020.

Since this was officially performed under protocol #056-2017 it was considered an "off-protocol" procedure and therefore we are reporting to OLAW with a copy to AAALAC. Of

note, we are actively gathering information regarding the lack of surgical proficiency in the other lab.

Sincerely,

(b) (6)

Randall S. Mason
Vice President, Research Operations

Cc: Principal Investigators
Chief of Endocrinology
IACUC Chair
IACUC Administrator
AAALAC, International

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, February 19, 2020 7:39 AM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: (b) (6)
Subject: RE: please see 1 attached letter

Thank you for providing this 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: Tuesday, February 18, 2020 3:51 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6)
Subject: please see 1 attached letter

Hello,

Please see the attached letter.

Sincerely,

(b) (6)

(b) (6)

Beth Israel Lahey Health 
Beth Israel Deaconess Medical Center

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Initial Report of Noncompliance

By (b) (6)

Date: 2/10/2020

Time: 11:00am

Name of Person reporting:

Telephone #:

Fax #:

Email:

Name of Institution:

Assurance number:

Beth Israel Deaconess Med. Cen.
A3153

Did incident involve PHS funded activity? Yes

Funding component: _____

Was funding component contacted (if necessary): _____

What happened? Mouse surgery performed that was not on protocol.

Species involved: Mouse

Personnel involved: Researcher

Dates and times:

Animal deaths: Yes

Projected plan and schedule for correction/prevention (if known): _____

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY

Case # _____