



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

May 18, 2021

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

Dr. Gyongyi Szabo
Chief Academic Officer
Beth Israel Deaconess Medical Center
330 Brookline Ave., (b) (4)
Boston, MA 02215

Dear Dr. Szabo,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your May 12, 2021 letter reporting a noncompliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals (Policy) within the animal care and use program at the Beth Israel Deaconess Medical Center (BIDMC). Your letter supplements information in the initial prompt telephone report on April 12, 2021. According to the information provided, OLAW understands that on March 5, 2021 the IACUC performed an inspection of an area where the research lab personnel perform procedures on mice. The related activity was PHS-funded. The following findings were reported:

- The room was found to be unkempt with a heavy smell of mouse urine.
- Numerous cages had been housed in the laboratory for several days and were extremely dirty, saturated with waste, and contained low amounts of chow.
- Approximately 20-30 cages containing mice were found covered in a blue drape, reducing air flow through the filter top.
- A number of the cages had lids designed to only be used on specific ventilated racks to insure adequate air flow.
- At least two of the cages housed sick mice that were hunched with ruffled fur, squinted eyes, and slow moving. At least two exhibited tremors that typifies mild seizure activity.

Corrective and preventive measures included euthanizing those animals that appeared moribund and moving the remaining animals back to the vivarium. All animal work will now be conducted inside the vivarium to allow vivarium staff to assist with monitoring.

OLAW appreciates the prompt consideration of this matter by Beth Israel Deaconess Medical Center, which was consistent with the philosophy of institutional self-regulation. Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate this incident, to take corrective actions, and prevent recurrence. OLAW concurs that the issue warranted reporting. We appreciate being informed of this matter and find no cause for further action by this office.

Page 2 -- Dr. Szabo
May 18, 2021
OLAW Case A3153-2R

Sincerely,

Brent C. Morse -S

Digitally signed by Brent C.
Morse -S
Date: 2021.05.18 16:13:13 -04'00'

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

cc: IACUC Contact

May 12th, 2021

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

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

Re: Non-compliance on Beth Israel Deaconess Medical Center (BIDMC) protocol #041-2016 titled "Genetic Contributors to Brain Tumorigenesis in the Mouse." and supported by NIH grants, R01 CA229784-01 under the title "Advancing treatment outcomes in malignant glioma by integrating immunotherapy and standard of care using genetically engineered mice that recapitulate molecular feature of human glioma" and R21 CA245337-01 under the title "Therapeutic vulnerabilities associated with PTEN missense mutations".

Dear Dr. Wolff:

The Institutional Animal Care and Use Committee (IACUC) sent a letter to a Principal Investigator (PI) on March 11, 2021 describing the findings of a semi-annual inspection completed on March 5, 2021 of (b) (4) of the BIDMC Dana building where the research lab personnel perform procedures on mice. The letter noted the following findings reported by the inspection team:

- In general, (b) (4) was found to be unkempt with a heavy smell of mouse urine. The floor was dirty with a significant amount of Enviro-Dri material and bedding on the floor. Used Innovive cages were found on a cart.
- Numerous cages had clearly been housed in the laboratory for several days and were extremely dirty, saturated with waste, and contained low amounts of chow. BIDMC policy as well as the protocol clearly state that animals are not to be housed greater than 24 hours outside the ARF.
- Approximately 20-30 cages containing mice were found covered in a blue drape. Covering cages reduces air flow through the filter top.
- A number of the cages were Innovive with ventilated lids and these lids are designed to only be used on specific Innovive racks to insure adequate airflow. In a static cage environment these lids are not appropriate. Of note, an Innovive housing rack was removed from the housing room on the morning of March 2nd, 2021 thus it was concluded that the cages that were found were not using the necessary racks for housing. The approved protocol states that appropriate housing will be used.
- At least two of the cages housed sick mice that were hunched with ruffled fur, squinted eyes, and slow moving, and at least two exhibited tremors that typifies mild seizure activity.

The PI was available and met with the IACUC inspectors and upon request, the moribund animals were euthanized that day and all other cages were moved back into the ARF. The laboratory space was also cleaned that day. The PI was made aware that he would be receiving a letter from the IACUC Chair and that a response to this letter was required and was to include a detailed explanation for the findings listed above and a plan moving forward. A letter from the PI was received in March 11th and shared with the committee.

330 Brookline Avenue
Boston, MA 02215
Tel: (b) (6)
gszabo1@bidmc.harvard.edu

The IACUC discussed at length the PI's response to the letter during the April 8th, 2021 normal monthly convened meeting. Overall, the committee found the letter to be inadequate and superficial citing lack of staff as the primary reason for the lack of oversight and concern for welfare.

After discussing the letter and taking into account the level of infractions, the IACUC unanimously decided that the PI's approval to perform animal work outside of the animal facility was to be rescinded immediately and for the foreseeable future. All animal work was to be moved inside the ARF to allow ARF staff to assist with monitoring. In addition, the IACUC requested that the PI send a revised response letter that agreed to the above decision and address why there had been an inability to maintain compliance with the policies, other than a lack of staff, and was to include a detailed plan explaining how the PI will prevent further non-compliance going forward.

A revised response letter was received and reviewed at the May 6th, 2021 IACUC meeting that was much more detailed (we would be happy to provide the response letter). He agreed to move his research operations inside the facility to ensure proper monitoring, acknowledging that help was needed. The committee was satisfied that a plan is in place to ensure animal welfare is maintained and that the PI now understands necessary compliance expected of him to be able to perform animal work and that this will prevent a similar incident from occurring in the future.

Sincerely,

(b) (6)

Gyongyi Szabo, MD, PhD
Chief Academic Officer/Institutional Official

Cc: Principal Investigator
IACUC Chair
IACUC Administrator
AAALAC, International

330 Brookline Avenue
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Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, May 14, 2021 7:19 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: letter

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

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

From: (b) (6)
Sent: Wednesday, May 12, 2021 12:57 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6)
(b) (6)
Subject: letter

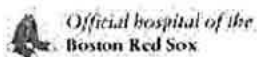
Good Afternoon,

Please see the attached letter.

Best,

(b) (6)

Beth Israel Lahey Health 
Beth Israel Deaconess Medical Center



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Initial Report of Noncompliance

By: BCM

Date: 4/12/2021

Time: Voicemail

Name of Person reporting: (b) (6)
 Telephone #: (b) (6)
 Fax #:
 Email:

Name of Institution: Beth Israel Deaconess
 Assurance number: A3153

Did incident involve PHS funded activity? yes
 Funding component:
 Was funding component contacted (if necessary):

What happened? Mice found housed in lab w/o IACUC approval and in substandard conditions. Some required euthanasia.

Species involved: Mus musculus
 Personnel involved: researchers
 Dates and times: ?
 Animal deaths: euthanized

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

Remaining mice moved to vivarium. Investigating.

Projected submission to OLAW of final report from Institutional Official:

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Case #