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CEDARS-SINAISM

Shlomo Melmed, MB, ChB., MACP, FRCP
Executive Vice President and Dean of the Medical Faculty
Helene A. and Philip E. Hixon Distinguished
Chair in Investigative Medicine
Director, Burns & Allen Research Institute

Transmit via E-mail

February 28, 2018

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

RE: Follow-up report of noncompliance regarding National Heart, Lung and Blood Institute (NHLBI) P01 HL112730 (CSMC IACUC Study Title: Mitochondrial Quality Control in Cardioprotection; CSMC IACUC #5000; Animal Species: Mice)

Dear Dr. Wolff:

In my capacity as the Institutional Official at Cedars-Sinai Medical Center (CSMC) (Assurance #D16-00420, Legacy #A3714-01), and in accordance with the PHS Policy on Humane Care and Use of Laboratory Animals (Policy) IV.F.3, I am writing this letter to provide a follow-up report regarding an incident of noncompliance and deviation from the provisions of the Guide for the Care and Use of Laboratory Animals (the *Guide*) related to the above-referenced NHLBI Grant. This case was previously reported to you by [REDACTED] IACUC Manager, Research Compliance and Quality Improvement at CSMC in a telephone conversation on February 7, 2018.

On January 18, 2018, during a semi-annual laboratory inspection, the subcommittee of the IACUC was granted access to the controlled substances double-lock box in a lab. The site visit team found expired Xylazine and Sodium Pentobarbital (both expired 11/2017) in the controlled substances lock box. The logbook data for these substances showed that they were used in mice after they expired. The member of the lab team was promptly informed by the IACUC sub-committee that administering expired anesthetics is strictly prohibited. The IACUC Chair followed-up by sending a memo to the PI on January 22, 2018, explaining that the use of expired anesthetics in animals is considered a serious deviation from the provisions of the *Guide* and requiring the PI to submit a corrective plan of action.

The PI responded on Thursday, February 1, 2018, confirming that the expired substances were used on 71 mice on her approved IACUC protocol #5000. 64 mice received expired xylazine and 7 mice received expired sodium pentobarbital. The PI discussed the matter at their laboratory meeting and instructed staff to double check the expiration date of all controlled substances prior to use. A new log was prepared, reiterating these instructions on the front cover, and the expiration date appears on the top of each log sheet. The PI confirmed that the expired xylazine and sodium pentobarbital had been disposed of. There were no indications that the use of expired substances resulted in any animal deaths or any other adverse outcomes.

At the convened IACUC meeting on February 19, 2018, the Committee accepted the PI's response and the actions taken to address this incidence of noncompliance. The IACUC placed the protocol on probation for a six-month period. During this time, if further problems occur, the PI and protocol may be subject to additional corrective actions. As of this date, the PI is complying with all stipulations mandated by the IACUC. The 6-month probationary period for the PI and the affected protocol is scheduled to end on August 20, 2018.

The study team verified that expenditures on the associated NHLBI grant related to this experiment amounted to a total of around \$2000, which would be reimbursed from the PI's institutional funds.

Please be assured that the institution considers the protection of laboratory animals to be of utmost importance. Please contact me at (b) (6) Dr. Denis Magoffin, IACUC Chair, at (b) (6), or (b) (6) at (b) (6) with any questions or concerns about this matter.

Sincerely, (b) (6)

Shlomo Melmed, M.D.

cc: Nina Hall, Grant Management Specialist, NHLBI
Kathryn Bayne, M.S., Ph.D., D.V.M., Global Director, AAALAC Int.
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Denis Magoffin, Ph.D., IACUC Chair, CSMC

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Principal Investigator of Record, CSMC

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, March 01, 2018 7:20 AM
To: [REDACTED]
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Cedars-Sinai Follow-Up Report of Non-compliance

Thank you for this report, [REDACTED] We will send a response soon.

Axel Wolff

From: (b) (6) [REDACTED]@cshs.org]
Sent: Wednesday, February 28, 2018 4:16 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Hall, Nina (NIH/NHLBI) [E] <nina.hall@nih.gov>; kbayne@aaaalac.org; Melmed, Shlomo, M.D. <Melmed@csmc.edu>; Magoffin, Denis, Ph.D. <Denis.Magoffin@cshs.org>; (b) (6) [REDACTED]@cshs.org>
Subject: Cedars-Sinai Follow-Up Report of Non-compliance

Dear Dr. Wolff,

Please find attached a letter from Dr. Shlomo Melmed reporting a non-compliance incident in research conducted at Cedars-Sinai Medical Center. Feel free to contact us with any questions or concerns.

Best,

(b) (6) [REDACTED]

CEDARS-SINAI
6500 Wilshire Blvd., Suite 1800 : Los Angeles, CA 90048
Main (b) (6) [REDACTED] : IACUC (b) (6) [REDACTED] : cedars-sinai.edu

**Follow-up report of noncompliance regarding National Heart, Lung, and Blood Institute Grant P01 HL112730 (CSMC
IACUC Study Title: Mitochondrial Quality Control in Cardioprotection; CSMC IACUC #5000; Animal Species: Mice)**

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Initial Report of Noncompliance

By: *an*Date: *2/1/18*Time: *11:00*Name of Person reporting: *(b) (6)**J Anne M...*Telephone #: *(b) (6)*

Fax #:

Email:

Name of Institution: *Cedar Sinai*Assurance number: *A3714*Did incident involve PHS funded activity? *yes*Funding component: *NHLBI*

Was funding component contacted (if necessary): _____

What happened? *Anesthetics**Expired controlled drugs found + had been used in mice (71)**No problems found with the mice*Species involved: *Mice*

Personnel involved:

Dates and times:

Animal deaths:

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

*Counsel lab staff, double check dates, new log book**Discard drugs*

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY

Case # _____