



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
Bethesda, Maryland 20892-7982
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

July 20, 2017

Re: Animal Welfare Assurance
#A3073-01 (OLAW Case D)

Andrew M. Welch, MHA, FACHE
Medical Center Director
New Mexico VA Health Care System
1501 San Pedro Drive SE
Albuquerque, NM 87108

Dear Mr. Welch,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your July 19, 2017 letter reporting an adverse event involving mice at the New Mexico VA Health Care System, following up on an initial telephone notification on June 27, 2017. According to the information provided, OLAW understands that 6 of the 12 knockout mice died unexpectedly following tamoxifen administration, exceeding the estimated 25% mortality rate. The IACUC determined that the observed elevated mortality may have been related to drug formulation since no mortality occurred when the study was repeated at a later date. The associated animal activity was not PHS funded.

The corrective actions consisted of reformulating the drug to ensure that all parameters, including concentration, purity, sterility and pH are appropriate; performing necropsies on mice that die following tamoxifen treatment in the future in an effort to discern the cause of death and enhancing vigilance regarding quality assurance in the preparation of agents that will be administered to mice.

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 being informed of these matters and find no cause for further action by this Office.

Sincerely,

(b)(6)

Neera V. Gopee, DVM, PhD, DACLAM, DABT
Animal Welfare Program Specialist
Division of Compliance Oversight

cc: IACUC Chair

(b)(6)

D.V.M., Chief Veterinary Officer, VA

(b)(6)



Department of Veterans Affairs
New Mexico VA Health Care System
1501 San Pedro Drive SE
Albuquerque, NM 87108-5154

In Reply Refer to: 501/151
Unexpected Study Outcome
Final Report
D16-00040 (A3073-01)

Dr. Neera Gopee
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
Bethesda, MD 20892-7982

RE: Assurance D16-00040 (A3073-01) - Unexpected Study Outcome

Dear Dr. Gopee:

As per our telephonic report on June 27, 2017, we had higher than expected mortality of mutant mice associated with an approved Tamoxifen dosing experiment conducted December 20, 2016 through January 6, 2017. This concern was reported and reviewed by the IACUC on January 10, 2017. Since we were uncertain about expected morbidity/mortality for this particular mutant strain, the committee requested refinement of the drug preparation and dosing methods to determine whether this outcome was inherent to the strain or due to methods. For this reason, we delayed reporting this unexpected event. However, based upon discussion with you and input from AAALAC site visitors on June 22, 2017, we recognize that we should have reported this at the time of the incident since mortality was not defined as an expectation in the approved protocol.

Unexpected Adverse Study Outcome

During an experiment in late December 2016 through early January 2017 when 12 conditional knockout mice were injected with Tamoxifen, 50% (6 total) either were euthanized due to morbidity or died. Although we were uncertain about expected outcomes for this genotype, mortality with this procedure for most strains is generally minimal and definitely not greater than 25%. The activity was not PHS funded.

Corrective Actions

During the initial IACUC review, January 2017, we were not sure what level of mortality might be expected with this particular genotype. For that reason, the committee requested that the PI: 1) reformulate the drug to assure concentration, purity, sterility,

pH and other parameters meet safety and efficacy standards; 2) allow the veterinarian the opportunity to conduct necropsies on future mice, if any, that die following tamoxifen dosing to determine whether cause of death is associated with drug toxicity effects or other potential causes.

Subsequent to reformulating, the experiment was repeated June 6 – 13, 2017 and all mice survived with no morbidity. The committee reviewed the outcome of the second experiment on July 11, 2017. The committee decided that the adverse outcome was likely related to the drug formulation. The IACUC requested that in the future the PI and laboratory staff assure more vigilance in quality assurance and preparations of agents for administration to animals.

If you have questions or need additional information, please contact (b)(6) at (b)(6) or by e-mail: (b)(6)@va.gov

Sincerely,

(b)(6)

Andrew M. Welch, MHA, FACHE
Medical Center Director
Institutional Official

cc: (b)(6) Ph.D., IACUC Chair
(b)(6) D.V.M., Chief Veterinary Officer, VA

(b)(6)

D16-00040 (A3073-01)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, July 19, 2017 11:47 AM
To: (b)(6)
Subject: RE: D16-00040 (A3073-01) Final Report

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

Axel Wolff, M.S., D.V.M.
Director, Division of Compliance Oversight
OLAW

From: (b)(6)@va.gov]
Sent: Wednesday, July 19, 2017 10:48 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b)(6)@va.gov>; (b)(6)@va.gov>; Fallon, Michael DVM PhD
(b)(6)@va.gov>; (b)(6)@va.gov>; (b)(6)@va.gov>
Subject: D16-00040 (A3073-01) Final Report

Hello Dr. Gopee,

Please see attached Final Report.

(b)(6)

New Mexico VA Health Care System
Albuquerque, NM

Phone: (b)(6)
Fax: (b)(6)
email: (b)(6)@va.gov



Initial Report of Noncompliance

By: Neera Gogel

Date: 6-27-17

Time: 3:34pm

Name of Person reporting:

(b)(6)

Telephone #:

(b)(6)

Fax #:

Email:

Name of Institution: New Mexico VAAssurance number: A3073-01Did incident involve PHS funded activity? Funding component: Was funding component contacted (if necessary):

What happened?

Mortality exceeded 50% after dosing 12 mice with tamoxifen.Species involved: Mice

Personnel involved:

Dates and times:

Animal deaths:

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

Projected submission to OLAW of final report from Institutional Official:

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Case #