



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) 402-7065

October 10, 2018

Re: Animal Welfare Assurance  
A3693-01 [OLAW Case H]

Dr. Keith LeJeune  
Senior Vice President for Research  
And Development  
Allegheny-Singer Research Institute  
320 East North Avenue  
Pittsburgh, PA 15212-4772

Dear Dr. LeJeune,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 28, 2018 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Allegheny Singer Research Institute, following up on an initial report on August 30, 2018. According to the information provided, OLAW understands that five mice died after receiving an unapproved drug in a bone marrow transplant/diabetes study. The drug posed a potential health risk to the animal care staff.

The corrective actions consisted of stopping the unapproved procedures, amending the protocol to include the drug but at a different dosing regimen, and retraining the Principal Investigator (PI) and staff on handling toxic agents. The PI and staff will verify all new drugs and procedures, will inform the facility staff, and will maintain communication with the Institutional Animal Care and Use Committee (IACUC), Attending Veterinarian, and the Pre-Clinical Facility Staff.

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.

Sincerely,

(b) (6)

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

cc: IACUC Chair



**Allegheny  
Health Network**

Allegheny Research Institute  
320 East North Avenue  
Pittsburgh, PA 15212-4722

September 28, 2018

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

RE: **Funding Source:** Internal  
**Name of Institute:** Allegheny Singer Research Institute  
**Assurance #:** D16-00408 (A3693-01)  
**PI:** Young Fan, Ph.D.  
**IACUC Application:** "Cell and Gene Therapy to Treatment of Type 1 Diabetes" (1055)

Dear Dr. Wolff,

This letter is offered in follow up to a preliminary report submitted by me to OLAW by phone on August 30, 2018 regarding a non-compliant event that occurred at the Allegheny Singer Research Institute (Assurance#: D16-00408). In short, the PI tested a preconditioning method for bone marrow transplantation that involved the use of a drug that was not listed in the approved IACUC protocol, resulted in the death of five mice that received the drug, and potentially exposed animal care staff to the metabolites of the drug. The noncompliance associated with these actions consisted of: conditions that jeopardize the health or well-being of animals; conduct of animal-related activities without appropriate IACUC review and approval; failure to adhere to IACUC-approved protocol; and implementation of any significant change to IACUC-approved protocols without prior IACUC approval.

Upon the PI self-reporting the issue, it was found that the use of a substance (Busulfan) was not approved by the IACUC and all animals expired (1 animal expired after the 2<sup>nd</sup> dose/day and 4 animals expired after the 3<sup>rd</sup> dose/day span). The PI described that he thought the Busulfan method of preconditioning was listed in the approved IACUC protocol and had the added benefit of avoiding the need for irradiation—however; neither the drug nor method was listed in the most current version of the protocol. The PI expressed that this was an unfortunate oversight and took responsibility for the noncompliance. He voluntarily discontinued the unapproved procedures.

The Committee discussed the full results of the investigation, including any potential risk to animal care and research staff members at the convened meeting on September 20, 2018, and determined that this was an isolated incident and not a programmatic failure. The committee accepted the following corrective action plan (CAP) that has since been implemented:

- The PI stopped all noncompliant activities immediately and submitted amendment to the IACUC for the use of the substance, including a revised dosing scheme based on AV recommendations and relevant literature.
- The PI and research staff received mandatory re-training in the areas of non-compliance including improvement in the orientation of new research staff members with regard to facility and protocol specific training. Training included the required labeling of cage cards following administration of a substance.

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Tuesday, October 09, 2018 6:23 AM  
**To:** Dawnmarie DeFazio  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Notification of noncompliance-Allegheny Singer Research Institute: D16-00408 (A3693-01)

Thank you for this report, Ms. DeFazio. We will respond shortly.  
Axel Wolff

**From:** Dawnmarie DeFazio [mailto:Dawnmarie.DEFAZIO@ahn.org]  
**Sent:** Friday, October 05, 2018 1:19 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** Keith Lejeune <Keith.LeJeune@ahn.org>; (b) (6) Krista Gibbs  
<Krista.Gibbs@AHN.ORG>; Kevin M. Kelly <Kevin.KELLY@ahn.org>; (b) (6)  
**Subject:** Notification of noncompliance-Allegheny Singer Research Institute: D16-00408 (A3693-01)

**Name of Institute:** Allegheny Singer Research Institute

**Assurance #:** D16-00408 (A3693-01)

To Whom It May Concern:

Attached please find the report of noncompliance regarding the determination of serious noncompliance by the IACUC for an internally funded animal protocol (#1055-PI: Yong Fan) for Allegheny Singer Research Institute (D16-00408 (A3593-01)). This was originally verbally reported.

If you have any questions, please let me know.  
Regards,  
Dawn

Dawnmarie DeFazio, CHRC, CIP

Director, Clinical Research and Regulatory Affairs

AHN Research Institute

Allegheny Health Network

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Dawnmarie.DeFazio@ahn.org

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## Initial Report of Noncompliance

By: ALW

Date: 8/30/18

Time: 12:45

Name of Person reporting: Kerth LeBeau, ID

Telephone #: (b)(6)

Fax #:

Email:

Name of Institution: Allegheny Singer Research Inst.

Assurance number: A3693

Did incident involve PHS funded activity? No

Funding component: \_\_\_\_\_

Was funding component contacted (if necessary): \_\_\_\_\_

What happened?

Bone marrow transplant protocol, used toxic drug on 5 mice + they died. Drug not on protocol

Species involved: Mice

Personnel involved:

Dates and times:

Animal deaths:

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

Stopped work, amend protocol, get IBC approval

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY

Case # \_\_\_\_\_