



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) 402-7063

April 10, 2019

Re: Animal Welfare Assurance  
A3544-01 [OLAW Case J]

Dr. Dennis Durbin  
Chief Scientific Officer  
Nationwide Children's Hospital  
700 Children's Drive – W177  
Columbus, Ohio 43205-2696

Dear Dr. Durbin,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 1, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Research Institute at Nationwide Children's Hospital, following up on an initial telephone report on March 21, 2019. According to the information provided, OLAW understands that a surgical procedure on one pig deviated from the approved protocol. Specifically, cells were placed into the intestine and a bypass loop was created in the intestine, although neither procedure had been approved. Intestinal contents subsequently leaked from the surgical site.

The corrective actions consisted of euthanizing the pig at the established humane endpoint. The responsible investigator's animal use privileges were suspended, the investigator was retrained, upon restoration of animal use privileges the investigator will be closely monitored, and the investigator was placed on probation. The animal activities were allowed to continue according to the approved protocol, the NIH grant was not charged for any unauthorized animal activities, and the Institutional Animal Care and Use Committee accepted the corrective actions.

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,

(b) (6)

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

cc: IACUC Chair



**NATIONWIDE CHILDREN'S**  
*When your child needs a hospital, everything matters.™*

April 1, 2019

Axel Wolff, DVM  
Director, Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
Rockledge 1, Suite 360  
6705 Rockledge Drive  
Bethesda, MD 20892

Dear Dr. Wolff:

The Research Institute at Nationwide Children's Hospital, in accordance with Assurance A3544-01 and PHS Policy IV.F.3., provides this report of noncompliance regarding one of our researchers performing a surgical procedure not approved on the IACUC protocol. I first reported this incident to you on March 21, 2019 via a telephone call.

One Animal Resource Core veterinary technician who was monitoring the pig during surgery noticed that the procedure varied from the previous 5 surgeries. The veterinary technicians reported the variation immediately to the Lead Veterinary Technician who reported it to Dr. Goodchild, the attending veterinarian. By the time Dr. Goodchild was apprised of the deviation, the surgery was completed.

The research is funded by NIH Grant: NIH STTR R42 DK107168 entitled "Production of Tissue Engineered Intestine". No charges from this incident have been applied to the NIH fund.

The purpose of the protocol is to develop engineered gut tissue for recovery from necrotizing enterocolitis, a devastating condition in preterm human infants. In brief, the procedure approved by the IACUC involved 2 surgeries. In the first surgery, a small section of gut is resected for isolation of cells as a source of engineered gut tissue. Cells are implanted on graft scaffolds. Scaffolds are implanted in the abdominal wall or wrapped in mesentery to generate engineered tissue. A second surgery performed one month later involves recovery of engineered gut cell scaffolds from the abdominal wall and implantation in line at a second site in the gut.

Surgery was carried out on five pigs following the procedure approved in the IACUC protocol. Surgery on the sixth pig carried out on February 28, 2019 deviated from the approved protocol. Briefly, cells recovered from resected gut were placed on the scaffolds and one was placed within the gut rather than the abdominal wall. To prevent stricture of the gut, a bypass loop was created in the intestine. This is a significant deviation from the approved protocol. The animal was euthanized on March 3, 2019 as it met humane endpoints defined in the IACUC protocol. Necropsy revealed leakage from the gut surgical site.

At the request of the IACUC, the PI barred the researcher from further work with animals pending resolution of the IACUC investigation and development of a remedial plan for the researcher. The researcher's card key access to the vivarium was suspended. It will be restored when a plan for remedial training and monitoring of future work with animals is instituted.

The following corrective action plan was implemented after the incident:

1. Completion of online AALAS training courses identified by the IACUC under supervision by the Director of Research Integrity.

2. Upon successful completion of AALAS courses, the researcher's work with animals will be supervised for three months under conditions defined by the IACUC.
3. Any serious violation of IACUC protocols or policies by the researcher in the next 12 months will be referred directly to Dr. Durbin, the Institutional Official, for action.

The protocol is not suspended as the non-compliant activity was carried out by the researcher who acted without informing the PI or other study staff. The PI voluntarily halted activity on the protocol until progress towards study goals is evaluated based on data from 5 pigs that were treated according to the approved protocol.

The PI lab has always been very conscientious with regards to protocols and activities. We believe our remediation steps will adequately address this issue.

At the IACUC meeting on April 1, 2019, the IACUC reviewed and accepted the corrective action plan. The IACUC determined that this was an isolated incident and not a programmatic failure.

Please do not hesitate to contact me if you require further information.

With regards,

 (b) (6)

Dennis Durbin, MD  
Institutional Official  
Chief Scientific Officer

**Morse, Brent (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Wednesday, April 10, 2019 9:06 AM  
**To:** (b) (6) OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** (b) (6) Durbin, Dennis  
**Subject:** RE: Final report from D16-00331

Thank you for providing this report. 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:** Monday, April 01, 2019 1:17 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** (b) (6) Durbin, Dennis  
<Dennis.Durbin@nationwidechildrens.org>  
**Subject:** Final report from D16-00331

Please see the attached Final Report.

The Research Institute at Nationwide Children's Hospital, in accordance with Assurance D16-00331 (old A3544-01) and PHS Policy IV.F.3., provides this final report of a noncompliance regarding an unapproved surgery. This was reported by telephone on March 21, 2019. At that time, you requested a written final report. The full IACUC met on April 1, 2019 and approved the attached report.

If you need any additional information, please let me know.

(b) (6)



**NATIONWIDE CHILDREN'S**  
*When your child needs a hospital, everything matters.*



## Initial Report of Noncompliance

By: *aw*

Date: *5/21/19*

Time: *8:00*

Name of Person reporting: *Dennis Durbin, I/O*

Telephone #: *(b)(6)*

Fax #:

Email:

Name of Institution: *Research Institute National Children's Hospital*

Assurance number: *A3544*

Did incident involve PHS funded activity? *Yes*

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

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

What happened?

*2 surgical procedures, intestine sfx, stem cells  
Didn't do as per protocol - leak in intestine, septic.*

Species involved: *Pi g*

Personnel involved:

Dates and times:

Animal deaths:

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

*Voluntary hold, euthanasia, prevent animal and personnel  
Training, enhanced oversight, take pictures*

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY

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