



DEPARTMENT OF HEALTH & HUMAN SERVICES

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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

January 27, 2023

Re: Animal Welfare Assurance
#A3272-01 [OLAW Case 2T]

Dr. Denis Wirtz
Vice Provost for Research
Johns Hopkins University
(b) (4) Garland Hall
3400 N. Charles St.
Baltimore, MD 21218

Dear Dr. Wirtz,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your January 24, 2023 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Johns Hopkins University, following up on an initial telephone report on September 11, 2022. According to the information provided, OLAW understands that a rabbit on an oncology study involving the liver became severely distressed and required euthanasia. It was determined that the tumor burden in the liver had exceeded the humane endpoint and veterinary consultation had not been sought for an animal in poor health. The tumor growth had been more aggressive than anticipated and there was metastases to the lung.

The corrective actions consisted of the Institutional Animal Care and Use Committee directing the laboratory to develop and implement a body condition scoring system and to adjust the time when imaging is conducted. The laboratory staff was trained on body scoring systems, on the appropriate conduct of health checks, on prompt reporting of animal concerns to the veterinarian, and was directed to consult experts regarding proper tumor implantation. The protocol was subsequently amended and all required training has been completed.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate, correct, and prevent recurrence of the noncompliance. Your prompt and thorough resolution of this matter is commendable and consistent with the PHS Policy philosophy of monitored self-regulation. We appreciate having been informed about this matter and find no cause for further action by this Office.

Sincerely,

(b) (6)

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

cc: IACUC Chair
Robert Gibbens, D.V.M., USDA-APHIS-AC



A3272-2T

January 24, 2023

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare
National Institutes of Health
Bethesda, Maryland 20892-6910

RE: Animal Welfare Assurance #A3272-01, OLAW Case 2T

Dear Dr. Wolff:

Please accept this letter as the final report on a finding of serious noncompliance with the Public Health Service (PHS) *Policy on Humane Care and Use of Laboratory Animals*. In accordance with federal guidelines, the circumstances in question were described to you in a prompt report from Dr. Brendan Canning, Chair of the Johns Hopkins University (JHU) Animal Care and Use Committee (ACUC) on September 11, 2022 (OLAW Case #A3272-2T).

The study in question involves implantation of VX tumors into the liver of rabbits with the goal of studying a treatment utilizing alpha particle bombardment of the cancerous growth(s). This particular tumor model is used extensively in cancer research, including many studies performed in rabbits, with multiple published papers describing the progression of tumor growth and metastasis that informed experimental design by the JHU scientists. The planned research had been described in a protocol that was reviewed and approved by the JHU ACUC. No federal funds were used to support these studies.

On September 1st a rabbit was found by veterinary residents and staff in severe distress, prompting humane euthanasia. The ACUC later determined after discussions with lab personnel that this was the first rabbit that had received image guided implantation of tumor fragments as described in the protocol. The tumor fragments had been implanted 2 weeks prior to euthanasia. Published literature had indicated that at 2 weeks tumor growth and metastasis would be minimal. No other animals had been implanted with liver tumors at the time of this intervention.

Pathology indicated that the animal had died with a poor body condition score, tumor burden in the liver that had exceeded protocol endpoint, ascites and metastases that had entered the lung. On September 6th an ACUC Compliance Subcommittee was held. The researchers presented published evidence supporting their belief that tumor burden should have been minimal 2 weeks after surgery but acknowledged a far more aggressive growth than anticipated as well as metastasis involving the lung. The lab presented records that documented daily monitoring of the rabbit both before and after tumor implantation. Based on the precedent of published literature, no imaging had yet been performed to assess tumor burden. The Compliance Subcommittee learned that a vet tech working for the group had noted poor health in the animal on the evening before euthanasia and had alerted a faculty member involved in the study. But no veterinary consult was sought that evening. The subcommittee voted unanimously that the care for this rabbit was inadequate, that the lab had exceeded stated endpoints for the study, and that the lab had not sought veterinary consult as expected in instances of poor health. Corrective actions included a recommendation that the lab develop and implement a body condition scoring system and to initiate imaging soon after tumor implant (the originally approved protocol narrative indicated that imaging to monitor tumor progression would begin 2 weeks after implantation). Additional recommendations included training of all lab members in the use of body scoring systems and the completion of health checks on rabbits, reinforcing the expectation that veterinary consults be requested when poor health is noted, and plans to rely on experts associated with the protocol to ensure proper tumor implantation. The results of the Compliance Subcommittee meeting were presented at the September 15th meeting of the

Office of the Provost

265 Garland Hall 3400 N. Charles Street Baltimore, MD 21218 410-516-8070 <http://web.jhu.edu/administration/provost>

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ACUC. The ACUC voted unanimously that the circumstances represented serious noncompliance. The ACUC also voted unanimously that the corrective actions recommended were appropriate. An amendment to the existing protocol has been submitted and approved and personnel have now completed all mandatory training. The ACUC considers this matter closed.

Please do not hesitate to contact me if you have additional questions.

Sincerely,

(b) (6)

Denis Wirtz, Ph.D.
Vice Provost for Research

cc: AAALAC International

Brendan J. Canning, Ph.D., Chair, Johns Hopkins University Animal Care and Use Committee
Eric Hutchinson, D.V.M., DACLAM, Attending Veterinarian and Assistant Vice Provost for Animal Research and Resources, Johns Hopkins University

(b) (6)

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, January 25, 2023 7:36 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD); Wolff, Axel (NIH/OD) [E]
Subject: RE: OLAW Final Report (case 2T)

Good morning (b) (6)

Thank you for sending us this final report for case A3272-2T and we will send an official response soon.

Best,
Devora

Devora McCoy, BS, MBA ([pronunciation](#))
Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Phone: 301-435-2390
Email: devora.mccoy@nih.gov

From: (b) (6)
Sent: Tuesday, January 24, 2023 4:04 PM
To: Wolff, Axel (NIH/OD) [E] <WolffA@OD.NIH.GOV>
Cc: Brendan Canning <bjc@jhmi.edu>; Eric Hutchinson <ehutchi8@jhmi.edu>; (b) (6) Denis Wirtz <wirtz@jhu.edu>
Subject: [EXTERNAL] OLAW Final Report (case 2T)

Dear Dr. Wolff,

On behalf of Denis Wirtz, please find a letter regarding the final report on case 2T, attached. (OLAW Case #A3272-2T)

(b) (6)

McCoy, Devora (NIH/OD) [E]

From: Brendan Canning <bjc@jhmi.edu>
Sent: Friday, December 30, 2022 12:14 PM
To: McCoy, Devora (NIH/OD) [E]
Subject: [EXTERNAL] Re: OLAW Case A3272-2T

Dear Devora,

Thanks for writing. As one of our corrective actions in this case we had implemented mandatory training focused on physical exam of the animals for all personnel involved. We were hoping to hear from our veterinarians that they could confirm competency in these tasks prior to submitting our final report. I would expect this training to be completed (along with our final report) within 2 weeks.

Thanks again all the best for 2023.

Brendan

Brendan J. Canning, Ph.D.
Professor of Medicine
Chair, Johns Hopkins University Animal Care and Use Committee
Johns Hopkins Asthma and Allergy Center
5501 Hopkins Bayview Circle
Baltimore, Maryland 21224
(b) (6)
e-mail: bjc@jhmi.edu

From: McCoy, Devora (NIH/OD) [E] <devora.mccoy@nih.gov>
Date: Friday, December 30, 2022 at 10:30 AM
To: Brendan Canning <bjc@jhmi.edu>
Cc: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>, Animal Care Use Committee <acuc@jhmi.edu>
Subject: OLAW Case A3272-2T

Good morning,

I'm contacting you regarding OLAW Case A3272-2T, concerning noncompliance with a tumor study. We originally received a preliminary report via phone call on 09-11-22. Can you please provide us with an update or final report for this case?

Thanks,
Devora

Devora McCoy, BS, MBA
Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare

National Institutes of Health
301-435-2390

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Initial Report of Noncompliance

By: (b) (6)

Date: 9/11/22

Time: 920

Name of Person reporting: Brendan Canning IACUC chair
 Telephone #: (b) (6)
 Fax #: (b) (6)
 Email: BJC@JHU.edu

Name of Institution: Johns Hopkins U
 Assurance number: A3272

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

What happened?

Liver Cancer study in rabbits. Tumor growth not monitored + tumors too big which impacted health.

Species involved: Rabbits

Personnel involved:

Dates and times:

Animal deaths:

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

Projected submission to OLAW of final report from Institutional Official:

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Case # _____