



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

March 6, 2020

Re: Animal Welfare Assurance
A3143-01 [OLAW Case 1A]

Dr. Camille P. Wicher
Vice President, Corp. Ethics and
Research Subject Protection
Roswell Park Cancer Institute
Elm & Carlton Streets
Buffalo, NY 14263

Dear Dr. Wicher,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 2, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Roswell Park Cancer Institute. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the Roswell Park Cancer Institute Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: the conduct of animal-related activities without appropriate IACUC approval. The final report states that an amendment was reviewed at the December 2019 monthly meeting requesting a change to a protocol to allow mice with ulcerated tumors no larger than 1 cm to be permitted on study. It is stated the committee recently approved protocols and amendments that permit mice with ulcerated tumors to be kept on experiment based on justification provided by the investigator and performance of a pilot experiment to demonstrate if the ulcers heal, and if so, the time frame. The IACUC decided to initiate a policy to address these requests using an evidence and performance-based approach. After discussion by the committee and review of the amendment to protocol, the IACUC requested additional information in order approve the amendment. It is stated that the amendment needs to include monitoring cards on cages of mice with an ulcerated tumor for veterinary review, and list a monitoring criteria that would require euthanasia. The committee also requested in the review of the amendment the data obtained from the pilot study for review at the February meeting of the IACUC. The committee detailed the specific data sets that should be submitted for review.

Prior to the February meeting, the IACUC received the revised amendment along with a report from a well-designed experiment that included dates of treatment, photographs, and measurements of the ulcerated tumors and graphs of animal weights throughout the duration of the experiment. The requested revisions to the amendment reviewed at the December meeting had not been submitted for DMR approval prior to the investigator conducting the pilot experiment. While the committee appreciated the valuable information provided, this was a non-compliance of the protocol. The committee at the February meeting reviewed the revised amendment along with the results of the pilot study and approved the amendment following minor revisions.

It is noted that the final report does not state if this project was supported by PHS funds. Based on its assessment of this explanation, OLAW understands that the Roswell Park Cancer Institute has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy. We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

(b) (6)

Jacquelyn T. Tubbs, DVM
Veterinary Medical Officer
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Chair

Tubbs, Jai (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, March 3, 2020 7:15 AM
To: Wicher, Camille; OLAW Division of Compliance Oversight (NIH/OD)
Cc: (b) (6) Moser, Michael
Subject: RE: Reports of non-compliance

Good morning Dr. Wicher,

Thank you for the reports. We will send an official response soon.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM
 Veterinary Medical Officer
 Office of Laboratory Animal Welfare
 National Institutes of Health

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From: Wicher, Camille <Camille.Wicher@RoswellPark.org>
Sent: Monday, March 2, 2020 4:20 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6) Moser, Michael <Michael.Moser@RoswellPark.org>
Subject: Reports of non-compliance

Please find two reports of non-compliance. Thank you.

Camille P. Wicher, Ph.D., Esq. MSN, RN
 Assistant Professor of Oncology
 Vice President
 Roswell Park
 Elm & Carlton Sts.
 Buffalo, New York 14263

(b) (6)



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Camille P. Wicher, Ph.D. Esq., RN, MSN.
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e-mail: camille.wicher@roswellpark.org

March 2, 2020

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

RE: Reports of Non-Compliance
OPRR Assurance #A-314301.
USDA Regis. #21-R-032

Dear Dr. Wolff,

Please accept the enclosed reports as required by 9 CFR 2.31 (c) (3) and (d) (7) Subchapter A of the Animal Welfare Act, as well as PHS Policy IV.F.3.

Corrective action has been instituted as per the attached document. Roswell Park Cancer Institute is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard. Should you have any questions, please do not hesitate to contact me at (b) (6)

Thank you in advance for your cooperation in this matter.

Sincerely,

(b) (6)

Camille P. Wicher, PhD., Esq., RN, MSN
Vice President
Institute Official



Michael T. Moser, Ph.D.
Chair Institutional Animal Care and Use
Committee (IACUC)
A457 Carlton House
Buffalo, NY 14263
Phone: 716 845-1155
FAX: 716 845-1258
Mike.Moser@roswellpark.org

(b) (6)

To: Camille Wicher, Ph.D., RPCI Institute Official
From: Michael T. Moser, Ph.D., Chair RPCI IACUC
DATE: February 27, 2020
Re: Non-Compliance with IACUC protocol 1368M: Ulcerated Tumor

This memo is to report a non-compliance animal welfare incident that occurred mid December 2019-mid January 2020. Although IACUC believes this was due to a misunderstanding between IACUC and the investigator, IACUC believes this constitutes an animal welfare concern and therefore may be reportable. An amendment for protocol 1368M from (b) (6) was reviewed at the December 2019 monthly meeting (12/03/2019) requesting a change to the protocol to allow mice with ulcerated tumor no larger than 1 cm be permitted on study. The current protocol and IACUC guidelines require that an ulcerated tumor be an endpoint. The amendment stated that:

"tumor specific immune responses induced in immunocompetent mice have a tendency to ulcerate in subcutaneously implanted tumors such as murine lymphoma cell line EL4. Other factors such as depth of injection and rate of growth can contribute also to tumor ulceration. Length of survival following therapy is critical to evaluating the success or failure of treatment. Ulcerated tumors may actually heal with treatment but will not be realized if mice are euthanized prematurely."

The committee has recently approved protocols and amendments that permit mice with ulcerated tumors to be kept on experiment provided the investigator provide justification and perform a pilot experiment to demonstrate if the ulcer heals, and if so, the time frame. Using this information, the IACUC determines if mice with ulcerated tumors are permitted for those protocols. In addition to previous requests from investigators using immunological approaches for treatment of tumor and resulting tendency to ulcerate but then heal as therapeutic treatment progresses, there were three separate requests in November and December to allow mice with ulcerated tumors to be kept on protocol. Given this, the IACUC decided to initiate a policy to address these requests using an evidence and performance-based approach. Therefore, after discussion by the committee and the review of the amendment to 1368M the IACUC requested the following information in order to approve the amendments. (designated member review):

The amendment needs to include a statement that monitoring cards will be placed on the cages of mice with an ulcerated tumor for veterinary review. The card would also list monitoring criteria that would require euthanasia:

1. signs of dehydration;
2. signs of an infection;
3. of pain; i.e. self-trauma;
4. bleeding ulceration;
5. if an ulcer reaches 1 cm in diameter
6. Weight loss of 20%
7. Body Score of 2 or less (see attached LASR SOP)
8. Signs of declining overall health are noted regardless of ulcer size.

The IACUC also requested in the review of the amendment:

"Please submit the data obtained from this pilot study for review at the February meeting of the IACUC. Data that should be submitted for review should include the measurements for all tumors vs ulcerations observed, how many mice had an ulceration, how many mice had to be euthanized, how many mice had ulcerations that healed or got smaller with treatment. Included in this data should be any information on weight loss of mice that recovered and those that had to be euthanized based on the above criteria. The IACUC is going to use this data along with that of other investigators to establish an evidence/performance-based policy for mice with ulcerated tumors and appropriate criteria to use for humane endpoints. If you have any questions, feel free to contact the IACUC Chair".

Prior to the February meeting, the IACUC received the revised amendment along with a report from a well-designed experiment that included dates of treatment, photographs and measurements of the ulcerated tumors, and graphs of animal weights throughout the duration of the experiment. The endpoints for the pilot study were those requested in the December IACUC review. The requested revisions to the amendment reviewed at the December meeting had not been submitted for DMR approval prior to the investigator conducting the pilot experiment (mid-December-January 2020). Although the IACUC appreciated the impressive design of experimental approach of the study and the valuable information provided this was a non-compliance of protocol 1368M and a possible animal welfare concern. In addition, the protocol did not include photography of animals.

The committee at the February meeting (02/04/2020) reviewed the revised amendment along with the results of the pilot study and approved the amendment following minor revisions after review of the pilot data (Designated member review).

The IACUC feels these non-compliances were a result of a misunderstanding by the investigator from the December 2019 review of the amendment. The IACUC believes the continued enrollment of mice with ulcerated tumors on study was a potential animal welfare issue that may be reportable. If you have any additional questions, require clarification or further action by the IACUC please feel free to contact me.