



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) 480-3387

January 6, 2023

Re: Animal Welfare Assurance  
A3823-01 [OLAW Case 10P]

Dr. Mary Dickinson  
Senior Vice President and Dean of Research  
Baylor College of Medicine- Houston  
One Baylor Plaza, MS BCM335  
Houston, TX 77030

Dear Dr. Dickinson,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your December 16, 2022 response to my December 9, 2022 request for additional information regarding an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Baylor College of Medicine. According to the information provided, OLAW understands the following:

- 1) The cause of morbidity/mortality experienced in mice receiving a low dose of lipopolysaccharide (LPS) could not be determined.
- 2) To reduce or eliminate morbidity/mortality, the laboratory will use a different agent which is approved in the protocol.
- 3) Should LPS be used in the future, its use will be monitored by a veterinarian.
- 4) Negative outcomes had not been expected in this study.
- 5) The protocol now addresses any potential negative outcomes due to use of LPS. Specifically, clinical signs are described as well as the monitoring schedule.
- 6) The NIH grant was not charged for any unauthorized animal activities.
- 7) Due to the change in agent, additional problems are not expected. Should LPS be used again, animals will be closely monitored.

Based on its assessment of this information, OLAW understands that measures have been implemented to correct and reduce the likelihood of a recurrence of the initial problem. OLAW concurs with the actions taken by the institution 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



## OFFICE OF RESEARCH

One Baylor Plaza, BCM310  
Houston, Texas 77030-3411

(713) 798 – 2104  
(713) 798 – 2721 FAX  
mdickins@bcm.edu

## CONFIDENTIAL

December 16, 2022

Brent Morse, DVM, DACLAM  
Director, Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
olawdco@mail.nih.gov

Dear Dr. Morse,

Thank you for your letter regarding OLAW Case A3823-10P, please find the following responses to your letter dated December 9, 2022:

1. What was the cause of the morbidity/mortality?  
*The cause of the morbidity and mortality is uncertain. Since Lipopolysaccharide (LPS) was given at a low concentration and dose (0.4-0.8 mg/kg, up to 200ul, IP), it is not clear that it caused the negative outcomes.*
2. Have any changes been made in the procedures or the agent to reduce or eliminate morbidity/mortality?  
*As a refinement to reduce future morbidity/mortality in case this was related to LPS, the laboratory has decided to use Poly-inosinic-poly-cytidylic acid (plpC) injections in place of LPS. Use of plpC is described in the approved protocol.*
3. Did the veterinarian identify any problems during oversight of the LPS administration?  
*There have not been any further injections with LPS. If the laboratory decides to use LPS again, administration and monitoring will be overseen by a Clinical Veterinarian.*
4. Were negative outcomes expected?  
*Negative outcomes were not expected.*
5. Does the protocol now include information about potential negative outcomes, if applicable?  
*Yes, negative outcomes have been outlined in the protocol: "Mice may display signs of distress following the injection of LPS due to endotoxemia, such as weight loss, reduced activity, and body condition (hunched posture and ruffled fur). These symptoms are typically resolved by 48 hours post treatment. Mice will be monitored daily before and twice daily after LPS injection for body weight, appetite changes, and body condition (hunched posture, ruffled fur, decreased mobility)."*
6. Confirm that the NIH grant was not charged for any unauthorized animal activities.  
*We confirm that the NIH grant was not charged for any unauthorized animal activities.*
7. Provide any additional information on this study and steps taken to reduce morbidity/mortality.  
*The laboratory is not planning on resuming LPS injections and instead plan to use plpC injections. If LPS is used in the future, close animal monitoring of the injections and treated animals will be conducted.*

As always, we greatly appreciate your guidance in our commitment to animal welfare. Please do not hesitate to contact me should you have any additional questions.

Sincerely,

(b) (6)

Mary Dickinson, PhD  
Sr. Vice President and Dean of Research  
Institutional Official  
Baylor College of Medicine

**McCoy, Devora (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Monday, December 19, 2022 7:51 AM  
**To:** (b) (6)  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: OLAW Case A3823-10P

Good morning (b) (6)

Thank you for sending us this additional information and we will send an official response soon.

Best,  
Devora

Devora McCoy, BS, MBA  
Program Analyst  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
301-435-2390

**From:** (b) (6)  
**Sent:** Friday, December 16, 2022 4:59 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** Dickinson, Mary <mdickins@bcm.edu>; (b) (6) McCoy, Devora (NIH/OD) [E] <devora.mccoy@nih.gov>  
**Subject:** [EXTERNAL] RE: OLAW Case A3823-10P

Good afternoon,  
Please find the response to Case A3823-10P, as requested, and sent on behalf of Dr. Mary Dickinson.

Please let us know if you have any additional questions or concerns.

Thank you,

(b) (6)

**From:** McCoy, Devora (NIH/OD) [E] <devora.mccoy@nih.gov>  
**Sent:** Friday, December 9, 2022 9:10 AM  
**To:** Dickinson, Mary <mdickins@bcm.edu>

**Cc:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>;

(b) (6)

(b) (6)

**Subject:** OLAW Case A3823-10P

Good morning Dr. Dickinson,

Attached please find Dr. Wolff's response to OLAW Case A3823-10P. Please note that additional information is being requested by December 31, 2022. If you have any questions, feel free to contact us by phone or by e-mail.

Best,  
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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December 9, 2022

Re: Animal Welfare Assurance  
A3823-01 [OLAW Case 10P]

Dr. Mary Dickinson  
Senior Vice President and Dean of Research  
Baylor College of Medicine- Houston  
One Baylor Plaza, MS BCM335  
Houston, TX 77030

Dear Dr. Dickinson,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your November 28, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Baylor College of Medicine. According to the information provided, OLAW understands that 16 mice had been given lipopolysaccharides (LPS) although this had not been approved in the protocol and led to four deaths and four moribund animals.

The corrective actions consisted of euthanizing the remainder of the mice and amending the protocol to include the agent. The laboratory staff was retrained, the Principal Investigator counseled the staff on the content of the protocol, and a veterinarian will oversee the next use of the agent in the mice. The laboratory was placed on enhanced post-approval monitoring.

While OLAW concurs with the proposed corrective actions, we request additional information as follows:

- 1) What was the cause of the morbidity/mortality?
- 2) Have any changes been made in the procedures or the agent to reduce or eliminate morbidity/mortality?
- 3) Did the veterinarian identify any problems during oversight of the LPS administration?
- 4) Were negative outcomes expected?
- 5) Does the protocol now include information about potential negative outcomes, if applicable?
- 6) Confirm that the NIH grant was not charged for any unauthorized animal activities.
- 7) Provide any additional information on this study and steps taken to reduce morbidity/mortality.

Please provide the requested information by **December 31, 2022**.

Sincerely,

(b) (6)

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

cc: IACUC Chair

**McCoy, Devora (NIH/OD) [E]**

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**From:** McCoy, Devora (NIH/OD) [E]  
**Sent:** Friday, December 9, 2022 10:10 AM  
**To:** mdickins@bcm.edu  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD); [REDACTED] (b) (6)  
**Subject:** OLAW Case A3823-10P  
**Attachments:** A3823-10P.pdf

Good morning Dr. Dickinson,

Attached please find Dr. Wolff's response to OLAW Case A3823-10P. Please note that additional information is being requested by December 31, 2022. If you have any questions, feel free to contact us by phone or by e-mail.

Best,  
Devora

Devora McCoy, BS, MBA  
Program Analyst  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
301-435-2390





## OFFICE OF RESEARCH

One Baylor Plaza, BCM310  
Houston, Texas 77030-3411

(713) 798 – 2104  
(713) 798 – 2721 FAX  
mdickins@bcm.edu

## CONFIDENTIAL

November 28, 2022

Brent Morse, DVM, DACLAM  
Director, Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
olawdco@mail.nih.gov

RE: Assurance #D16-00475

Dear Dr. Morse,

As Institutional Official for Baylor College of Medicine (BCM), I have the duty to inform you of our Institutional Animal Care and Use Committee's (IACUC) recent findings in animal research after an assessment of the following protocol:

**Protocol:** AN-5858: Stem Cells in Development and Aging

**Species:** Mice

**Funding Sources:** National Cancer Institute (NCI) R01-CA255813, R01-CA193235, National Heart, Lung and Blood Institute (NHLBI) R01-HL165145 and Non-PHS Funding

For this investigator's first incident of this nature, the IACUC determined that the following finding constituted *serious noncompliance*<sup>1</sup> with the federal regulations:

*8/31/2022 – Animals were given an unapproved substance*<sup>2</sup>

A Clinical Veterinarian was notified to evaluate several cages of mice with health concerns. He observed four mice that were moribund and four mice that were dead, that were treated with lipopolysaccharides (LPS), which was not described in the IACUC approved protocol. There were 16 total mice that were given the LPS and the remaining mice were euthanized. An amendment to add the LPS and related procedures to the protocol was submitted and subsequently approved by the IACUC.

*11/8/2022 – Determination at a fully convened IACUC meeting*

To protect the welfare of animals and prevent future recurrence, the IACUC required following corrective actions:

1. All research personnel are required to complete the interactive "Top 10 Pitfalls in Animal Research and how to Avoid Them" training.
2. The PI is required to review the protocol with all research members, to ensure everyone understands the protocol completely.
3. A Clinical Veterinarian will observe and monitor animals following the next treatment with LPS.

<sup>1</sup> PHS Policy IV.F.3.a: "The IACUC, through the Institutional Official, shall promptly provide OLAW with a full explanation of the circumstances and actions taken with respect to: a. any serious or continuing noncompliance with this Policy;"

<sup>2</sup> PHS Policy IV.B.7i: "...the IACUC shall with respect to PHS-conducted or supported activities: review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities..."

4. One comprehensive Post-Approval Monitoring (PAM) review focused on LPS injection and animal monitoring will be conducted within the next three months.

This finding of non-compliance does not appear to pose any potential or actual effect on costs related to this PHS-supported research.

This notification will also be sent to AAALAC International, the NCI, the NHLBI and the non-PHS funding source according to the terms and conditions of the award.

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

Sincerely,

(b) (6)

Mary Dickinson, PhD  
Sr. Vice President and Dean of Research  
Institutional Official  
Baylor College of Medicine

cc: Principal Investigator  
Department Chair  
Research Compliance Services files

**McCoy, Devora (NIH/OD) [E]**

---

**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Tuesday, November 29, 2022 12:49 PM  
**To:** (b) (6)  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: OLAW Reports- Assurance D16-00475

Good afternoon (b) (6)

Thank you for sending us these three reports and we will send official responses soon.

Best,  
Devora

Devora McCoy, BS, MBA  
Program Analyst  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
301-435-2390

**From:** (b) (6)  
**Sent:** Tuesday, November 29, 2022 10:38 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** (b) (6)  
**Subject:** [EXTERNAL] OLAW Reports- Assurance D16-00475

Dear Dr. Morse,

Please find the attached notifications of research non-compliance as determined by our IACUC, and sent on behalf of Dr. Mary Dickinson, Institutional Official.

Please feel free to contact me if you have any questions.

Thank you,

(b) (6)

