



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

November 7, 2022

Re: Animal Welfare Assurance
A3494-01 [OLAW Case F]

Dr. Ian Colrain
President and Chief Executive Officer
Midwest Research Institute
425 Dr. Martin Luther King Jr. Blvd
Kansas City, MO 64110

Dear Dr. Colrain,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your October 28, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at MRIGlobal, following up on an initial report on August 25, 2022. According to the information provided, OLAW understands that rabbits on an ocular study received eyedrops which had a pH range that differed from what had been described in the approved protocol. The pH had not been checked prior to application and the rabbits displayed mild eye irritation. The study was funded through the Biomedical Advanced Research and Development Authority under contract 75A50121C00030.

The corrective actions consisted of checking the pH, determining that the data was not usable due to the incorrect formulation, and euthanizing all 32 rabbits involved. The laboratory staff was directed to follow established internal procedures and quality control measures when preparing experimental compounds, the Study Director was directed to provide appropriate instruction to staff via communication and in the protocol, and all staff involved in the project must be knowledgeable about the content of the protocol prior to starting the work. The Institutional Animal Care and Use Committee approved an amendment to this protocol using Full Committee Review. The Client has performed pH stability testing on the eye drops, has shared this data with MRIGlobal, and has outsourced the dose formulation for future studies.

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

cc: IACUC Chair
Nina El-Badry, BARDA
Robert Gibbens, D.V.M., USDA-APHIS-AC



The science you expect.
The people you know.

Ian Colrain, PhD
CEO, Institutional Official
icolrain@mriglobal.org

A3494-F

October 28, 2022

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

Dear Ms. McCoy:

MRIGlobal, in accordance with Assurance A3494-01 and PHS Policy IV.F.3., provides this report of noncompliance regarding an incident in which rabbits were mis-dosed. The study Animal Use Statement (AUS), entitled "Preliminary Proof of Concept Study: Treatment of Sulfur Mustard Induced Ocular Injury using aCT1 Eye Drops," was assigned No. 21-18. This incident was officially reported to the OLAW Division of Compliance Oversight, on August 25, 2022 via email from Elizabeth "Lizzie" Morrison, IACUC Chair.

On July 29, 2022, the IACUC received Incident Report No. 22-04, which indicated that rabbits were mis-dosed. Per the AUS and client-provided formulation procedure, rabbits should have received eye drops with pH in the range of 6-6.5. During formulation of the eye drops, performed by MRIGlobal, the pH was not checked. When rabbits displayed mild eye irritation following dosing with the eye drops, the dose formulation was investigated, including the pH, which was determined to be between 5-5.5. The Study Director and Client determined that any further data from the study would be unusable due to the incorrect formulation being given to the animals. Therefore, the decision was made, in consultation with the attending veterinarian and IACUC chair, to euthanize the animals to prevent unnecessary pain and distress. The IACUC investigated the incident and requested corrective actions from the Study Director.

This project is funded through the Biomedical Advanced Research and Development Authority under contract 75A50121C00030, where MRIGlobal serves as a subcontractor to the prime awardee.

To address this specific situation, immediate actions were taken.

1. As noted previously, the mis-dosed animals were euthanized to prevent unnecessary pain or distress.
2. The IACUC investigated the incident and made the following recommendations:
 - a. Staff were directed to follow MRIGlobal internal documents for formulation preparations and data QC procedures.
 - b. Study Director was directed to provide adequate communication to staff performing work on the study.
 - c. Study Director needs to provide clear specifications/outcomes in the Study Protocol.
 - d. Study Protocol needs to be fully executed and reviewed by all staff involved in

- the project prior to work being conducted.
3. The IACUC requested full committee review of any AUS amendment made to continue work on this program.
 4. The Study Director and Client developed a plan to prevent future animal welfare incidents from occurring on this study. The Client has performed pH stability testing on their formulation and provided the data to MRIGlobal. The Client will be outsourcing the dose formulation portion of future studies.

The study AUS was amended, and a full committee review was conducted prior to approval. The Study Director provided satisfactory responses to all IACUC comments.

MRIGlobal 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 regarding this report, please contact Lizzie Morrison, IACUC Chair.

Thank you for your consideration of this matter.

Sincerely,

(b) (6)

Ian Colrain, PhD
CEO
Institutional Official
MRIGlobal

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, November 1, 2022 11:02 AM
To: Morrison, Lizzie
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Initial Report of Noncompliance

Hi Lizzie,

No problem and thanks for your quick response. We will continue to review this report and an official response will be sent 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: Morrison, Lizzie <lmorrison@mriglobal.org>
Sent: Tuesday, November 1, 2022 10:59 AM
To: McCoy, Devora (NIH/OD) [E] <devora.mccoy@nih.gov>
Cc: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: [EXTERNAL] RE: Initial Report of Noncompliance

Good morning,

I apologize for the oversight. I used the report template on the OLAW website and neglected to update that section. Attached is the corrected report.

Lizzie

From: McCoy, Devora (NIH/OD) [E] <devora.mccoy@nih.gov>
Sent: Monday, October 31, 2022 4:04 PM
To: Morrison, Lizzie <lmorrison@mriglobal.org>
Cc: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: RE: Initial Report of Noncompliance

Good afternoon Lizzie,

I was reviewing this report and noticed that the assurance number documented in the report doesn't match the assurance number we have listed for your institution. The report has A0101-01, but I believe it should read A3494-01. Is it possible to have this corrected and sent back to us?

Thanks,
Devora

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

From: Morrison, Lizzie <lmorrison@mriglobal.org>
Sent: Monday, October 31, 2022 10:50 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: [REDACTED] (b) (6)
Subject: [EXTERNAL] RE: Initial Report of Noncompliance

Good morning,

Attached you will find the completes investigation report.

Please let me know if you have any questions,
Lizzie

From: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Sent: Friday, August 26, 2022 6:44 AM
To: Morrison, Lizzie <lmorrison@mriglobal.org>
Cc: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: RE: Initial Report of Noncompliance

Good morning Lizzie,

Thank you for sending us this preliminary report and we look forward to receiving the final report once the investigation is complete.

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: Morrison, Lizzie <lmorrison@mriglobal.org>
Sent: Thursday, August 25, 2022 5:51 PM

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

Cc: (b) (6)

Subject: [EXTERNAL] Initial Report of Noncompliance

Good afternoon,

As the IACUC Chair at MRIGlobal, I am writing to file an initial report of noncompliance.

- Name and contact information of person reporting: Lizzie Morrison, IACUC Chair, (b) (6)
- Name of institution: MRIGlobal
- Assurance number: D16-00309(A3494-01)
- Funding component and if contacted (for situations related to PHS-supported activities): BARDA, our client has notified BARDA of the issue.
- Brief description of incident (e.g., species, category of personnel involved, dates, times, animal deaths): 32 rabbits were exposed to sulfur mustard (HD) on 7/25/2022 and began test article treatment the same day, consisting of twice daily eye drops. On study day 3, 7/28/2022, the study director was made aware that the eyedrops were not tested for pH after formulation. The pH was immediately tested and it was found that the low dose group (Group 2) pH was 5.55, and the mid (Group 3) and high (Group 4) dose groups were both at 5.09. The eyedrops pH should have been 6-7.4. This was concerning given the corneal epithelium was injured by HD in the right eye of the animals. The attending veterinarian and client were consulted. It was concluded that there would be no valuable data acquired from this study, and the animals should be humanely euthanized. The attending veterinarian and IACUC chair were contacted to make a quick decision to euthanize all 32 animals.
- Plan and schedule for correction and prevention (if known): An IACUC investigation into this incident was immediately started and will be used to identify corrective actions.
- Timeframe for final report from the Institutional Official: A completed report should be submitted within 60 days of this initial notification.

Please don't hesitate to contact me with any questions,



The science you expect.
The people you know.

Lizzie Morrison, RBP, RQAP-GLP

Sr. Biosafety Officer/Responsible Official
IACUC Chair

Phone: (b) (6) Cell: (b) (6)

425 Dr. Martin Luther King Junior Blvd., Kansas City, MO 64110

www.mriglobal.org

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A3494-F

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, August 26, 2022 7:44 AM
To: Morrison, Lizzie
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Initial Report of Noncompliance

Good morning Lizzie,

Thank you for sending us this preliminary report and we look forward to receiving the final report once the investigation is complete.

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: Morrison, Lizzie <lmorrison@mriglobal.org>
Sent: Thursday, August 25, 2022 5:51 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: [REDACTED] (b) (6)
Subject: [EXTERNAL] Initial Report of Noncompliance

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Please don't hesitate to contact me with any questions,



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The people you know.

Lizzie Morrison, RBP, RQAP-GLP
Sr. Biosafety Officer/Responsible Official
IACUC Chair

Phone: (b) (6) **Cell:** (b) (6)
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