



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

September 15, 2021

Re: Animal Welfare Assurance
A3368-01 [OLAW Case 11J]

Dr. Nadine Connor
Associate Vice Chancellor
for Research Policy and Compliance
University of Wisconsin-Madison
(b) (4) Bascom Hall – 500 Lincoln Drive
Madison, WI 53706

Dear Dr. Connor,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your August 25, 2021 letter in response to the July 16, 2021 letter sent from this Office.

Additional information was requested after OLAW received a letter from Rise for Animals (Rise) regarding animal welfare concerns at the Wisconsin National Primate Research Center (WNPRC) at the University of Wisconsin-Madison. As stated in the previous letter, Rise reviewed the College of Letters and Science and Vice Chancellor for Research and Graduate Education Center's (LSVC) Animal Care and Use Committee meeting minutes for February 21, 2020, obtained through a Wisconsin Open Records Act request. Rise reported incidents that resulted in blood collection exceeding the maximum allowable volume within 30d. It was also stated that WNPRC staff responsible for the incident were to be trained on the procedure for blood collection. Your letter provides additional details on regarding several topics of interest to OLAW.

It is understood the protocol entitled "Defining infant outcomes following Zika virus infection" involves pregnant macaques being infected subcutaneously with Zika virus and hearing, ocular, and MRI exams are performed in offspring to determine if *in utero* exposure to Zika results in hearing, vision, or structural brain abnormalities. On January 21, 2020, infant rhesus macaque r19099 underwent protocol-approved hearing and ocular examinations. The following day, the same infant also underwent an MRI exam and 6mL of blood was collected for detection of Zika virus RNA and to perform a Zika virus antibody assay. On January 23rd, the room containing r19099's enclosure underwent routine sanitization. As a result, all the animal enclosures were temporarily moved and the enclosure in which r19099 lived with his mother was relocated from its typical position to a different one.

On January 23, 2020 a different animal, infant r19101, was scheduled to undergo ocular and MRI exams under the same IACUC-approved protocol. Since r19099's enclosure had been moved to the location where r19101's enclosure had previously been located prior to the room sanitization process, a WNPRC animal caretaker mistakenly removed r19099 for testing instead of r19101. It is understood that during the transfer process, the animal caretaker and research support staff members did not observe the mother's chest or leg tattoo or the infant's ear tattoo to verify they had the correct animal. As a result, infant r19099 underwent a 6mL blood collection, ocular exam, and an MRI was initiated before the animal care technician supervisor discovered that the incorrect animal had been transported to the imaging facility.

Per the report, this event is an isolated incident and under this protocol 40 rhesus macaque offspring exposed to Zika virus *in utero* have successfully undergone 259 experimental exams. It is understood that 30 MRI exams, and 29 ocular exams have been conducted successfully since the misidentification occurred with no additional incidents. It is also understood that no similar incidents of misidentification have occurred on any other protocol at the WNPRC.

On February 5, 2020, infant r19099 had 2mL of blood collected for major histocompatibility (MHC) testing. The report states the electronic health records system tracks expected blood volume across a 30-day period and is intended to prevent personnel from scheduling blood draws that would exceed 20% of an animal's blood volume in that time frame. In this instance, the veterinary staff responsible for scheduling the MHC blood draw for r19099 failed to check the animal's available blood volume for collection and did not enter the 2-mL blood draw until after it occurred. As a result, 1.4mL of blood was overdrawn from infant r19099 for the 30-day period. This finding was detected when the blood collection was entered, and an "overdrawn alert" was generated by the electronic health system. Per the report, the error in blood collection did not result in adverse clinical signs for the animal. It has been determined that the blood overdraw is the only instance that took place at the WNPRC since February 2020, and the WNPRC staff have completed more than 32,000 blood collections occurred during this time frame.

Per the report, standard operating procedures (SOPs) for animal identification, tattooing ID numbers and postpartum examination and infant processing outline the procedures staff use to properly identify nonhuman primates at the WNPRC. All macaques living at the WNPRC receive a six-letter alpha-numeric ID number when they are born or arrive at the center. Typically, the ID number is placed on their ears, chest, and inner left thigh of each macaque. Also, an individual metal medallion imprinted with an ID number is hung on the outside of each enclosure for each animal living within the enclosure.

It is noted that WNPRC staff are trained to verify the tattoo ID number of the animal they are transferring prior to removing the animal from its enclosure. Following the incident with infant r19099, all macaques are tattooed on the skin of the chest and inner left thigh when they reach a body weight of approximately 1kg. Additional corrective actions involved counselling and retraining of all individuals involved in these incidents. As stated in the July 16th letter, OLAW acknowledges that since this study is not PHS-funded, therefore, the events were not reported to this Office.

OLAW appreciates the prompt consideration of these matters by the WNPRC at the University of Wisconsin-Madison in providing our Office with this letter. We especially want to recognize your part as Institutional Official in providing transparency between your office and OLAW. We appreciate your cooperation regarding this matter and find no cause for further action by this Office.

Sincerely,

Jacquelyn T.
Tubbs -S

Digitally signed by
Jacquelyn T. Tubbs -S
Date: 2021.09.15 09:52:55
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Jacquelyn Tubbs, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact
Robert M. Gibbens, DVM, Director, Animal Welfare Operations



**Office of the Vice Chancellor for
Research and Graduate Education**
UNIVERSITY OF WISCONSIN-MADISON

August 25, 2021

Jacquelyn Tubbs, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

Dear Dr. Tubbs,

I write in response to your letter of July 16, 2021, regarding concerns raised by Rise for Animals. You requested: (1) information on how an animal was misidentified, (2) a statement indicating whether any similar incidents have occurred since February 2020, (3) a description of the animal identification program/practice at Wisconsin National Primate Center (WNPRC), (4) information regarding how WNPRC personnel are trained to identify animals, and (5) whether there is any redundancy for animal identification built into the program. Below please find UW-Madison's response to your inquiries.

1. Description of incidents and statement regarding lack of similar incidents

A. Misidentification

In IACUC-approved protocol G006108 (Defining infant outcomes following Zika virus infection), pregnant macaques are infected subcutaneously with Zika virus around gestation Day 45 and hearing, ocular, and MRI exams are performed in offspring to determine if *in utero* exposure to Zika results in hearing, vision, or structural brain abnormalities.

On January 21, 2020, infant rhesus macaque r19099 underwent these hearing and ocular examinations per the IACUC-approved protocol. The infant also underwent an MRI exam on January 22, 2020. On January 22, 2020, 6 mL of blood was also collected from infant r19099 to look for Zika virus RNA and to perform a Zika virus antibody assay.

On January 23, 2020, the room that held r19099's enclosure underwent mandated bi-weekly sanitization. During this process, all the animal enclosures were temporarily moved and the enclosure in which r19099 lived with his mother was rolled from its typical position at the right of the entrance door of the room to a position immediately to the left of the entrance door.

On January 23, 2020, infant r19101 was scheduled to undergo ocular and MRI examinations under the same IACUC-approved protocol (G006108). However, r19099's enclosure had been rolled to the location where r19101's enclosure had previously been located prior to the room sanitization process and a WNPRC animal caretaker mistakenly removed r19099 for testing instead of r19101. During the transfer process, the animal caretaker and research support staff members did not check the mother's chest or leg tattoo or the infant's ear tattoo to verify they had the correct animal. Subsequently, r19099 underwent a 6-mL blood collection, ocular exam, and an MRI was initiated before the animal care technician supervisor realized that the incorrect animal had been transported to the imaging facility.

Office of the Vice Chancellor for Research and Graduate Education

333 Bascom Hall 500 Lincoln Drive Madison, Wisconsin 53706 608-262-1044

This was an isolated incident that does not characterize the program. Since IACUC protocol G006108 was initiated, 40 individual rhesus macaque offspring exposed to Zika virus in utero have successfully undergone a total of 259 experimental examinations (100 hearing exams, 80 MRI exams, and 79 ocular exams). Thirty hearing exams, 30 MRI exams, and 29 ocular exams have been performed successfully since the misidentification incident with no additional incidents. Furthermore, no similar misidentification incidents have been recorded on any other protocols at the WNPRC.

B. Blood overdraw

On February 5, 2020, r19099 had 2 mL of blood collected for major histocompatibility (MHC) testing, crucial for verifying each rhesus macaque's susceptibility to simian immunodeficiency virus. This testing is generally performed early in an infant rhesus macaque's life at the WNPRC to determine if they will be maintained in the breeding colony or slated for future assignment to an infectious disease project.

The WNPRC maintains a strict protocol to limit the amount of blood that can be drawn from each individual animal in the colony per month (protocol 4.01 – Blood Sampling), based on an animal's estimated blood volume by body weight. Our electronic health records system tracks expected blood volume across a 30-day period and is intended to prevent personnel from scheduling blood draws that would exceed 20% of an animal's blood volume in that time frame.

Veterinary staff responsible for scheduling the MHC blood draw for r19099 failed to check the animal's available blood volume for collection and did not enter the 2-mL blood draw until after it occurred. This resulted in the animal being overdrawn for the 30-day period by 1.4 mL, which was detected when the blood collection was entered, and the electronic health records system generated an "overdraw alert." Fortunately, this did not result in adverse clinical effects for the animal, whose wellbeing was monitored daily by veterinary staff.

This blood overdraw described in this letter is the only instance that took place at the WNPRC since February 2020. During this period, WNPRC staff have completed more than 32,000 blood collections.

2. Description of animal identification program/practice, training, and redundancies

Standard operating procedures (SOPs) 1.01 (Animal Identification), 1.10 (Tattooing ID Numbers), and 3.05 (Postpartum Examination and Infant Processing) thoroughly outline the procedures staff use to properly identify nonhuman primates living at the WNPRC. All macaques living at the WNPRC receive a six-letter alpha-numeric ID number in our electronic health records system when they are born or arrive at the Center. Traditionally, this ID number is placed on their ears, chest, and inner left thigh of each macaque. Additionally, an individual metal medallion imprinted with an ID number is hung on the outside of each enclosure for each animal living within the enclosure.

WNPRC staff are trained to verify the tattoo ID number of the animal they are transferring (WNPRC SOP 1.02 – Animal Transport) prior to removing the animal from its enclosure. Prior to the incident with r19099, infant macaques received only ear tattoos at one to two weeks of age and did not receive tattoos of their ID numbers on their chest and inner thigh until they were weaned at 10-12 months of age; now all macaques are tattooed on the skin of the chest and inner left thigh when they reach a body weight of approximately one kilogram. Notably, we will soon pilot the placement of subcutaneous ID microchips in infant macaques (a process already in place in our marmoset colony) to complement chest/thigh tattoos and eliminate the need for ear tattoos.

All individuals involved with the described incidents were counseled regarding their errors and retrained using pertinent WNPRC SOPs. Because this was non-PHS-funded study, we did not report the above events to OLAW, however, as noted in your letter, these events were reported to the IACUC. The personnel of the WNPRC Animal Services Division remain dedicated to maintaining an exemplary level of care for our nonhuman primate populations.

We have included for your review the WNPRC SOPs referenced in this document. Please note that limited information has been redacted from the SOPs to protect personnel, animals, facilities, equipment, and other resources.

Please let us know if you have any additional questions.

Sincerely,

(b) (6)

Nadine P. Connor, Ph.D.
Professor and Oros Family Chair in Communication Sciences & Disorders
Associate Vice Chancellor for Research Policy & Compliance
Institutional Officer

xc:

(b) (6)

Janet Welter, PhD, DVM

(b) (6)



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Telephone: (301) 496-7163
Facsimile: (301) 480-3387

July 16, 2021

Re: Animal Welfare Assurance
A3368-01 [OLAW Case 11J]

Dr. Nadine Connor
Associate Vice Chancellor
for Research Policy and Compliance
University of Wisconsin-Madison
(b) (4) Bascom Hall – 500 Lincoln Drive
Madison, WI 53706

Dear Dr. Connor,

The Office of Laboratory Animal Welfare (OLAW) has received a letter from Rise for Animals (Rise) regarding animal welfare concerns at the Wisconsin National Primate Center (WNPR) at the University of Wisconsin-Madison.

Rise reviewed the College of Letters and Science and Vice Chancellor for Research and Graduate Education Center's (LSVC) Animal Care and Use Committee meeting minutes for February 21, 2020, obtained through a Wisconsin Open Records Act request. The following events were reported to OLAW from the obtained document:

- On January 21, 2020, an infant rhesus macaque, assigned to a protocol underwent an ocular exam, blood collection and MRI scan associated with the protocol.
- On January 23, 2020, the same animal underwent sedation, ocular exam, blood collection, intubation, and relocation to an MRI suite before it was determined the infant was the incorrect animal. WNPRC personnel that were responsible for the error were retrained in animal identification procedures (per the meeting minutes).
- On February 5, 2020, the same infant was sedated for routine physical exam, TB testing, and blood collection for a procedure (major histocompatibility complex typing) associated with the protocol.

The letter states the 3 events resulted in blood collection exceeding the maximum allowable volume within 30d. It is also reported that WNPRC staff responsible for the blood collection exceeding the maximum volume were to be trained on the procedure.

Although this project is not PHS-funded, OLAW is investigating to determine if a programmatic failure has occurred at the institution. Please clarify how the animal was misidentified and state whether similar incidents have occurred since February 2020. We request a description of the animal identification program/practice at the WNPRC. We also request information regarding how WNPRC personnel are trained to identify animals and if there is any redundancy for animal identification built in the program. Please provide an update to this Office by **August 30, 2021**.

Sincerely,

Jacquelyn T.
Tubbs -S

Jacquelyn Tubbs, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

Digitally signed by Jacquelyn T.
Tubbs -S
Date: 2021.07.16 11:08:50 -04'00'

cc: IACUC Contact

From:

(b) (6)

Sent: Monday, July 12, 2021 1:34 PM

To: Brown, Patricia [OLAW] (NIH/OD) [E] <brownp@od.nih.gov>; Laboratory Animal Welfare, Office of (NIH/OD) <OLAW@OD.NIH.GOV>

Subject: WNPRC Failure to Follow Procedure

Good afternoon,

Attached please find correspondence regarding the WNPRC's failure to follow proper procedure. Thank you for your attention to this important matter.

(b) (6)

Tubbs, Jai (NIH/OD) [E]

From: Morse, Brent (NIH/OD) [E]
Sent: Thursday, July 15, 2021 4:18 PM
To: Tubbs, Jai (NIH/OD) [E]
Subject: FW: WNPRC Failure to Follow Procedure

Follow Up Flag: Follow up
Flag Status: Flagged

Hi Jai,

Please include the email from Pat into the case file. Thanks.

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Brown, Patricia [OLAW] (NIH/OD) [E] <brownp@od.nih.gov>
Sent: Thursday, July 15, 2021 3:58 PM
To: (b) (6)
Cc: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Subject: RE: WNPRC Failure to Follow Procedure

Dear Ms. Chrzan,

This is in response to your communication of July 12, 2021 concerning The Wisconsin National Primate Research Center. At this time your concerns are under review by the Division of Compliance Oversight. OLAW takes seriously all noncompliance with the PHS Policy, either self-reported by the institution or received from other sources. Thank you for your concern regarding appropriate procedures for the humane care and use of laboratory animals in HHS-supported research.

Sincerely,

Patricia Brown, VMD, MS, DACLAM (she/her)
Director, Office of Laboratory Animal Welfare,
Office of Extramural Research,
Office of the Director, NIH
6700B Rockledge Drive
Bethesda, MD 20892-6910
301-496-7163
brownp@mail.nih.gov



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Walker, Keri (NIH/OD) [E]

From: Morse, Brent (NIH/OD) [E]
Sent: Tuesday, July 13, 2021 3:49 PM
To: Walker, Keri (NIH/OD) [E]
Cc: Tubbs, Jai (NIH/OD) [E]
Subject: FW: WNPRC Failure to Follow Procedure
Attachments: OLAW UW-Madison 71221.pdf

Follow Up Flag: Follow up
Flag Status: Completed

Keri,

Please use the attached and this email to open a case for A3368 and assign it to Dr. Tubbs. Thank you.

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Brown, Patricia [OLAW] (NIH/OD) [E] <brownp@od.nih.gov>
Sent: Tuesday, July 13, 2021 8:06 AM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Subject: FW: WNPRC Failure to Follow Procedure

Good morning Brent,
Please review this correspondence and determine whether an investigation is warranted. Once you have reviewed, I will acknowledge its receipt.
Thanks,
Pat

From: (b) (6)
Sent: Monday, July 12, 2021 1:34 PM
To: Brown, Patricia [OLAW] (NIH/OD) [E] <brownp@od.nih.gov>; Laboratory Animal Welfare, Office of (NIH/OD) <OLAW@OD.NIH.GOV>
Subject: WNPRC Failure to Follow Procedure

Good afternoon,

Attached please find correspondence regarding the WNPRC's failure to follow proper procedure. Thank you for your attention to this important matter.

All the best,

(b) (6)

Rise for Animals.

333 Washington Street, Suite 850, Boston, MA 02108

riseforanimals.org

July 12, 2021

Patricia A. Brown, VMD, MS
Director
Office of Laboratory Animal Welfare (OLAW)
National Institutes of Health
6700B Rockledge Dr., Suite 2500, MSC 6910
Bethesda, Maryland 20892
Via email: brownp@od.nih.gov; olaw@mail.nih.gov

Dear Director Brown:

On behalf of Rise for Animals (Rise), I am writing to relay our concern regarding troubling evidence of animal suffering at the Wisconsin National Primate Research Center (WNPRC) at the University of Wisconsin-Madison (UW-Madison), PHS Assurance #D16-00239 (A3368-01), of which you should be aware.

Document We Reviewed

In formulating the recommendation below, Rise reviewed the College of Letters and Science and Vice Chancellor for Research and Graduate Education Center's (LSVC) Animal Care and Use Committee (ACUC) [meeting minutes](#) for February 21, 2020, obtained through a Wisconsin Open Records Act request.

Finding: A Baby Monkey Was Inappropriately Used in a Procedure

The document we reviewed reveals that on January 21, 2020, an infant rhesus macaque, assigned to protocol G006108, underwent an ocular exam, blood collection, and MRI scan associated with protocol G006108.

Two days later, on January 23, 2020, the same infant underwent sedation, an ocular exam, blood collection, intubation, and relocation to an MRI suite "before it was discovered that it was the incorrect animal." According to the minutes, the WNPRC personnel responsible for the mistake were retrained on animal identification procedures.

Then, on February 5, 2020, "the same infant was sedated for a routine physical exam, TB testing, and blood collection for major histocompatibility complex (MHC) typing," associated with protocol G006108.

Thus, due to these three instances, blood collection exceeded the 20% allowable volume within 30 days. The WNPRC staff responsible for exceeding the maximum volume were to be trained on the procedure for blood collection. Protocol G006108 was not PHS-funded, and the ACUC accepted the report.

Request: OLAW Investigate the Situation

In reviewing this record, Rise was disappointed to see that OLAW was not made aware of these two failures to follow procedure at the WNPRC resulting in a baby monkey undergoing three procedures, as opposed to two, and having more than the maximum volume of blood collected within 30 days. Lab personnel failed to follow the animal identification standard operating procedure on January 23, 2020, resulting in several unauthorized medical procedures being performed. Then they failed to adhere to blood collection procedure on February 5, 2020, resulting in more than 20% of the infant's blood being drawn within a mere fifteen days. Rise wants to ensure that OLAW knows of this serious situation.

Further, we respectfully request that OLAW look into this failure at the WNPRC. While Protocol G006108 was not PHS-funded, the WNPRC is and as such, Rise requests that OLAW investigate this situation to ensure it does not occur again.

Thank you for your consideration of this request, and for your attention to this matter.

Sincerely,

(b) (6)

