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

August 14, 2023

Re: Animal Welfare Assurance
#A3012-01 [OLAW Case 1J]

David Mu, Ph.D.
Associate Dean for Research Administration
Eastern Virginia Medical School
735 Fairfax Avenue
EVMS Waitzer Hall, (b) (4)
Norfolk, VA 23507

Dear Dr. Mu,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your July 31, 2023 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Eastern Virginia Medical School (EVMS). This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this office understands that the EVMS Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to the conduct of animal activities without prior IACUC review and approval. The final report states the United States Department of Agriculture (USDA) identified noncompliance at EVMS during its May 2-3, 2023 routine inspection of the central animal facility and clinical records as documented in the USDA APHIS Inspection Report dated June 9, 2023. The findings relate to activities performed under an IACUC-approved protocol supported by NIH grants. The USDA APHIS Inspection Report included one noncompliant item with 3 specific findings.

The first finding in the USDA APHIS Inspection Report notes the protocol described blood sampling for all animals on the pregnancy studies (adult female olive baboons) to be performed under ketamine sedation at 2–4-day intervals, based on the treatment group. In 2023, the daily treatment records for animal #07105 showed the primate underwent daily blood draws during multiple time periods without the 2–4-day interval between collections. In 2021, the daily treatment records for animal #26876 revealed the animal also underwent daily blood draws during time periods that exceeded the 2–4-day interval between collections.

The final report states the investigator maintains the use of "2-4 day interval" meant that blood would be collected for 2-4 consecutive days followed by at least a one-day recovery period (i.e., no blood collection), rather than a rest period of 2-4 days between consecutive blood draws. It is also stated the protocol notes that the total volume of blood collected from an individual animal during a one-month period would not exceed 10% of the animal's total blood volume. Per the final report, the documented blood collections were within the allowable limit approved by the IACUC. However, the institution acknowledges based on the definition of the term interval, the protocol required the animals to be rested for 2-4 days between blood draws.

The second finding pertains to the protocol's description that all animals (adult female baboons) will be weighed monthly when they are on study. The protocol stated that animal weight is to be monitored weekly while the animal is on study, and the animal will be sedated. Per the USDA inspection report, the records of 5 female baboons on the current protocol only had weights documented during the semiannual exam and TB test or during a surgical procedure. When the USDA requested additional documentation of animal weights during this study period, none could be provided by the facility.

The final report states both the investigator and the institution recognize that animals were not weighed as outlined in the IACUC-approved protocol. It is also stated the 5 animals identified by USDA were regularly monitored by both the investigative and animal care staffs. None of the animals experienced clinically derived adverse events that could have been detected by weight loss, per the final report. However, the institution acknowledges failure to weigh animals as per the protocol, disregarded a clinical parameter and created a potential risk for avoidable clinical outcomes, pain, and/or distress.

The final finding pertains to an anticipated adverse event (seizures) described in the protocol and the steps to be taken for animals identified as nonresponsive, actively seizing, or unconscious. The inspection report states a 16yr old female olive baboon was discovered unresponsive by a technician on the morning of June 16, 2023. It is also stated there were no records indicating treatment was provided as outlined in the protocol. However, there is an entry from the Attending Veterinarian (AV) stating the animal was found unresponsive but by the time of the AV's arrival, the animal had eaten apples and was quiet, alert, and responsive.

Per the final report, investigators are asked to consider possible adverse events that may occur and to provide acceptable treatment plans. However, the institution relies upon the medical expertise of the AV to treat or to instruct the veterinary care staff regarding treatment of an animal in an emergent situation. It is understood that EVMS maintains the animal described in question was successfully managed at the discretion of the AV. It is noted the protocol does not state that the steps described must be implemented, nor does it supersede the professional opinion of the AV. The final report notes when the animal was found unresponsive, the animal care staff contacted the AV and during the conversation the animal became more responsive. The AV instructed the technician to provide apples to increase blood glucose, and the animal was found to be quiet, alert, and responsive upon the AV's arrival ~90min later. It is understood this information is documented in the medical record, and the animal was monitored throughout the day. No additional adverse events occurred regarding this animal, per the final report.

Various measures have been implemented in response to these findings. In summary, the actions taken by EVMS include the following:

- In February 2023, the institution's formal Post-approval Monitoring (PAM) program has been enhanced by expanding the scope of the audits. The program now includes a thorough review of applicable records, including the IACUC-approved protocol, research-related study documents, and veterinary clinical records. During the PAM records review, the auditor will discuss with the investigative staff the requirement for an amendment to a protocol to be approved by the IACUC prior to its implementation. All active protocols are audited at least annually, but more frequent audits may be conducted.
- The IACUC and Division of Comparative Medicine (CompMed) hosted a town hall on May 18, 2023 and attendance was mandatory for users authorized to work with USDA-regulated

species. Various animal care and use topics, including federal and institutional requirements for protocol approval and amendments to approved protocols were addressed during the session.

- The IACUC endorsed the AV's recommendation for a pre-implementation meeting (PIM) with the AV, the CompMed program manager, PAM personnel, the investigative staff, and/or IACUC Office staff. A PIM will be held prior to the start of a research protocol that is new to the EVMS animal care and use program or within 30 days of approval of a de novo renewal of an existing research project. It may also be extended to recently approved amendments to an approved protocol. The intent is to ensure that all involved parties are clear on the details of the protocol, discuss documentation requirements, ensure that required forms are sufficient to document proposed activities, and address any concerns raised by attendees.
- EVMS has purchased a new electronic medical recordkeeping system that will allow for standardization and enhanced oversight of clinical records. It is designed for day-to-day and ongoing management of individual animals and animal groups within a veterinary care setting. Also, investigators may use the system to monitor body weight trends and endpoint parameters for an added measure of compliance at the study level. Per the report, the institution hopes to implement use of the system within the next several weeks.

It is noted the USDA conducted another routine inspection of the central animal facility on July 12, 2023, and no noncompliance items were identified. Please be advised that it is your institution's responsibility to report these incidents to the funding institute's Chief Grants Management Officer and to make sure that no expenses related to these noncompliant activities are charged to the grant.

Based on its assessment of this explanation, OLAW understands that the Eastern Virginia Medical School has implemented 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,
Jacquelyn T. Tubbs -S
Digitally signed by Jacquelyn T. Tubbs -S
Date: 2023.08.14 08:14:22 -04'00'
Jacquelyn Tubbs, DVM, DACLAM
Senior Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact
(b) (6)

A3012-IJ

EVMS
Eastern Virginia Medical School

July 31, 2023

Brent C. Morse, D.V.M., DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare (OLAW)
National Institutes of Health (NIH)
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, Maryland 20892

Dear Dr. Morse:

RE: Report of Noncompliance
Eastern Virginia Medical School (EVMS), Norfolk, Virginia
Animal Welfare Assurance Number D16-00007

I am writing to inform OLAW of noncompliance identified by the United States Department of Agriculture (USDA) during its May 2-3, 2023 routine inspection of the EVMS central animal facility and clinical records and documented in the USDA inspection report dated June 9, 2023. This report is submitted in accordance with PHS Policy IV.F.3 and NIH guidance document NOT-OD-05-034, *Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals*. The findings relate to activities performed under IACUC-approved protocol #21-003, entitled *Regulation of Fetal-Placental Development in the Primate*, which involves a non-human primate (Papio Anubis/cynocephalus) model and is supported by the following NIH grants: HD 093070 and DK 120513. The NIH funding agency officials are copied on this report.

The noncompliant item (NCI) is classified by the USDA as a repeat occurrence, since EVMS was cited for violation of Animal Welfare Act (AWA) §2.31(c)(7) in the January 19, 2023 inspection report submitted in follow-up to the January 12, 2023 routine inspection. The January 2023 report states that the protocols referenced in that document were closed and no longer active at the time of the inspection.

The June 9, 2023 inspection report includes one NCI with three specific findings related to AWA §2.31(c)(7). Specifically, the report states that "IACUC approval is not being secured prior to enacting significant changes in protocol #21-003 regarding the care and use of animals in ongoing activities." The findings include the following occurrences taken directly from the USDA report:

- **USDA FINDING #1:** The protocol describes blood sampling for all animals on the pregnancy studies (adult female olive baboons) as being performed under ketamine sedation at 2-4 day intervals, depending on the treatment group. In 2023, the daily treatment records for animal #07105 ("Alyssa") show that she underwent daily blood draws during multiple time periods without a 2-4 day interval between collections. In 2021, the daily treatment records for animal #26876 ("Jemma") show that she also underwent daily blood draws during time periods that exceeded a 2-4 day interval between collections. Increased blood draw frequency can have potential impacts on animal health and well-being and is a significant change to the current IACUC-approved protocol.

Research
735 FAIRFAX AVENUE, WAITZER HALL - SUITE 1112
NORFOLK, VA 23507
TEL 757.446.8480
www.evms.edu

EVMS Response: The investigator maintains that his team's use of "2-4 day interval" meant that blood would be collected for 2-4 consecutive days followed by at least a one-day recovery period (i.e., no blood collection), rather than a 2-4 day rest period between consecutive blood draws. Additionally, the IACUC-approved protocol states that the total volume of blood collected from an individual animal during a one-month period will not exceed 10% of the animal's total blood volume. Based upon the documented initial weight of each animal, they would have to be bled 31-32 and 34 consecutive days, respectively, to exceed 10% of their total blood volume. Likewise, 29-30 consecutive days of blood collection would be required to exceed 10 mL/kg/month based upon each animal's average weight while on study. The animal treatment records confirm that neither animal was bled every single day for any given month; therefore, the documented blood collections were within the allowable limit approved by the IACUC. Although animal records support the investigator's intent to bleed the animals based upon his interpretation of "2-4 day interval" and document that neither animal was bled beyond the limit approved by the IACUC, the Institution acknowledges Merriam-Webster dictionary's definition of interval as *a space of time between events or states*; therefore, as written, the protocol requires the animals to be rested for 2-4 days between blood draws.

- **USDA FINDING #2:** The protocol states that all animals (adult female baboons) will be weighed monthly when they are on study. It later states that animal weight is monitored weekly while the animal is on study, and the animal will be sedated. Records of five female baboons on the current protocol only have weights documented during their semi-annual physical and TB test or during a surgical procedure. Upon request, no further documentation of animal weights during this study period could be provided by the facility. Monitoring the animal's weight weekly is described in the protocol as a clinical parameter to be monitored to indicate adverse effects, pain, and/or distress to the animals. Failure to follow the protocol and significantly decreasing the frequency of weigh-ins without IACUC approval does not allow the IACUC to review a change in the study procedure, especially one that is directly related to monitoring animal health and welfare.

  EVMS Response: The investigator and the Institution acknowledge that animals were not weighed as outlined in the IACUC-approved protocol. The five animals identified in the USDA report were regularly monitored by the investigative staff and the Division of Comparative Medicine (CompMed) animal care staff, and none of the animals experienced clinically derived adverse events that could have been identified by weight loss. However, the Institution understands that failing to weigh the animals as approved disregarded an important clinical parameter related to the overall health and well-being of the animals and created the potential risk for avoidable clinical outcomes, pain, and/or distress.

- **USDA FINDING #3:** The protocol describes an anticipated adverse event ("seizures") in approximately 10% of animals receiving a study drug from days 100-170 of gestation. Due to this known adverse event, the protocol documents steps that will be taken for animals found non-responsive, actively seizing, or unconscious which includes removing the animal from the cage, performing a blood gas analysis and glucose level, catheter placement and potential supplementation of dextrose depending on the blood glucose result. A 16-year-old female Olive baboon (#26876, "Jemma"), while receiving the study drug, was found unresponsive at 6 am by a technician on June 16, 2021. There are no records indicating treatment was provided as outlined in the protocol. The only entry is from the attending veterinarian (AV) stating that she was found unresponsive at 6 am but by the time the AV arrived she had consumed some apples and was up and quiet, alert, and responsive.

- **EVMS Response: Although investigators are asked to consider possible adverse events that could occur during the course of a study and to provide acceptable treatment plans for those events, the Institution ultimately relies upon the medical expertise of the AV to treat an animal directly or to instruct the veterinary care staff on how to treat an animal in an emergent situation. EVMS maintains that the cited incident was managed successfully at the discretion of the AV and in the best interest of the animal's well-being following an adverse health event. With respect to Letrozole administration, the IACUC-approved protocol states that the sudden onset of seizures at approximately Days 120-150 of gestation (i.e., approximately 20-50 days of Letrozole treatment), is possible in approximately 10% of animals assigned to the study. It further states that, in that case, the animal typically is found lying down in its cage early in the morning, suggesting that the seizure likely occurred overnight or very early that morning. Early intervention is important, since it may be more difficult to revive the animal the longer it goes without treatment. IACUC #21-003 outlines a recovery procedure that "seems most relevant to implement" in the event of a suspected seizure. The protocol does not say that the procedure must be implemented, nor does it state that it supersedes the professional opinion of the AV. In this particular case, as relayed to the IACUC by the AV at the time of the incident, when Jemma was found unresponsive the morning of June 16, 2021, the care staff contacted the AV, per standard protocol. During the conversation between the technician and the AV, Jemma became more responsive. As instructed by the AV, the technician gave Jemma apples to elevate her blood glucose level, as an immediate treatment measure until the AV was on-site to assess and continue treatment, as applicable. Jemma was alert enough to eat the apples and responded to the initial treatment. When the AV arrived approximately 90 minutes later, she was quiet, alert, and responsive, as documented in the medical record. To have followed the suggested recovery protocol and sedate an animal that was responsive and exhibiting normal behaviors would have been contraindicated per the professional medical opinion of the AV at the time of the incident. As stated in the protocol, a responsive animal is to be returned to its cage and monitored throughout the day. Jemma responded immediately; therefore, she was allowed to remain in her cage, where she was monitored throughout the day. No additional adverse events occurred; therefore, Jemma was allowed to remain on study.**

IACUC #21-003 is the current 3-year renewal of a peer-reviewed, federally funded research project that has been underway for decades. We attribute the success of the surgeries performed to date and the overall well-being of animals assigned to the project to the excellent care and management provided by the investigative and veterinary care staff and to the coordinated oversight provided by the IACUC.

To address the concern that investigators are enacting significant changes to ongoing activities without securing IACUC approval prior to implementation, the Institution has implemented the following measures:

1. **Enhanced Post-approval Monitoring (PAM):** As of February 2023, the institution's formal PAM program has been enhanced by broadening the scope of the audits, increasing the number of PAM professionals conducting the audits, and expanding the logistics of the auditing process. Originally, PAM audits focused primarily on the conduct of IACUC-approved procedures. In additional to procedural audits, the enhanced program includes a thorough review of applicable records, including the IACUC-approved protocol, research-related study

documents, and veterinary clinical records. During the PAM records review, the auditor verbally discusses with the investigative staff the requirement for an amendment to a protocol to be approved by the IACUC prior to implementation of the amended activity. Additionally, the auditor informs the staff that failure to comply with this requirement constitutes noncompliance that will be reported to OLAW, the USDA, and/or the protocol funding agency, as applicable. Additionally, the written report sent to the principal investigator (PI) following the PAM audit includes a statement informing the investigator of the same. All active protocols are audited at least one a year, although more frequent audits may be conducted at the discretion of the IACUC, the AV, the PAM auditors who act on behalf of the IACUC, and/or the Institutional Official (IO).

2. **Town Hall:** On May 18, 2023, the IACUC and CompMed hosted a 2-hour Town Hall, which addressed a number of animal care and use topics, including federal and institutional requirements for protocol approval and amendments to approved protocols. All authorized animal users were invited to attend; however, attendance was mandatory for users authorized to work with USDA-regulated species, to include the CompMed staff. The Town Hall was well attended and all required users were present. Going forward, the IACUC and CompMed will continue to provide written information/reminders to the research community regarding proper management of IACUC-approved protocols. Additionally, the IACUC has discussed hosting semi-annual Town Halls to keep investigators abreast of federal regulations and updated guidance, current institutional policies and procedures, adequate recordkeeping, industry trends and best practices, and other related/relevant topics.

3. **Pre-implementation Meeting (PIM):** At its July 6, 2023 meeting, the IACUC endorsed the AV's recommendation for a pre-implementation meeting (PIM) with the AV, the CompMed program manager, PAM personnel, the investigative staff, and/or IACUC Office staff. A PIM will be held prior to the start of a research protocol that is new to the EVMS animal care and use program or within 30 days of approval of a de novo renewal of an existing research project. It may also be extended to recently approved amendments to an approved protocol. The intent of the PIM is to ensure that all involved parties are clear on the details of the protocol, to discuss documentation requirements, to ensure that required forms, such as a post-operative monitoring form, are sufficient to document the proposed activities, and to discuss other questions/concerns raised by an attendee. The desired goals of the PIM are to increase effective communication between the research community, the IACUC, and the CompMed staff and to obviate the potential for noncompliance related to off-protocol activities.

4. **ZIMS Medical Records System:** EVMS has purchased a new electronic medical recordkeeping system that will allow for standardization and enhanced oversight of clinical records and will, in turn, promote consistency and compliance within the animal care and use program. The Species360 Zoological Information Management System (ZIMS) is designed for day-to-day and ongoing management of individual animals and animal groups within a veterinary care setting. In particular, ZIMS for Medical is the cloud-based platform within the Species360 ZIMS that captures and catalogues anesthesia, treatment, diagnostic testing, clinical observation, and related medical records. It may also be used to search and retrieve clinical data and to integrate medical and drug regulatory compliance records, all of which will help to improve and enhance communication among the veterinary staff. Additionally, investigators may use the system to monitor body weight trends and endpoint parameters for an added measure of compliance at the study level. ZIMS for Medical may be used as a

stand-alone resource or it may be integrated with other ZIMS platforms, such as ZIMS for Husbandry, to create a more comprehensive records management resource. The institution hopes to receive and implement use of ZIMS for Medical within the next several weeks.

On July 12, 2023, the USDA conducted another routine inspection of our central animal facility, veterinary records, and IACUC documentation. No noncompliant items were identified during that inspection.

EVMS is committed to ensuring the humane care and use of animals involved in its animal care and use program and to maintaining compliance with PHS Policy and the USDA AWA. The Institution believes that the measures described above will greatly aid our investigators, the CompMed staff, and the IACUC to that end. As always, EVMS appreciates any guidance and assistance provided by OLAW.

Please do not hesitate to contact me should you have questions and/or concerns regarding this report.

Sincerely,

(b) (6)

David Mu, Ph.D.
Associate Dean for Research Administration/Institutional Official
EVMS Office of Research
735 Fairfax Avenue
Waitzer Hall, (b) (4)
Norfolk, Virginia 23507
(b) (6)
MuD@evms.edu

DM/cbh

cc: John V. Ilekis, NIH Program Official, NICHD
Corinne M. Silva, NIH Program Director, NIDDK
Principal Investigator
Alireza Hosseini, M.D., EVMS IACUC Chair
Tara S. Reilly, D.V.M., cVMA, EVSMS CompMed Attending Veterinarian
(b) (6)

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, July 31, 2023 4:00 PM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: EVMS #D16-00007 - NONCOMPLIANCE REPORT

Good afternoon (b) (6)

Thank you for sending us this report 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: Monday, July 31, 2023 2:11 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Ilekis, John (NIH/NICHD) [E] <ilekisj@mail.nih.gov>; Silva, Corinne (NIH/NIDDK) [E] <silvacm@niddk.nih.gov>; Mu, David <MuD@EVMS.EDU>; (b) (6) Hosseini, Alireza <HosseiA@EVMS.EDU>; Reilly, Tara S. <ReillyTS@EVMS.EDU>; (b) (6)
(b) (6)
Subject: [EXTERNAL] EVMS #D16-00007 - NONCOMPLIANCE REPORT
Importance: High

Dear Dr. Morse:

RE: Noncompliance Report
Eastern Virginia Medical School (EVMS), Norfolk, Virginia]
Animal Welfare Assurance Number D16-0007 (formerly A3012-01)

The attached report is sent on behalf of David Mu, Ph.D., Associate Dean for Research Administration and Institutional Official. The NIH funding agency officials are copied. A copy of the report will be sent to the Principal Investigator under separate cover. Please do not hesitate to contact me or Dr. Mu if you have questions about or require additional information regarding this report.

Kindest regards,
(b) (6)

(b) (6)

[redacted]

A3012-1J

USDA

United States Department of Agriculture

Animal and Plant Health Inspection Service

4700 River Road
Riverdale, MD 20737

June 15, 2022

William J. Wasilenko, Ph.D.
Vice Dean for Research and Institutional Official
EVMS Office of Research
735 Fairfax Avenue
Waitzer Hall, (b) (4)
Norfolk, Virginia 23507

Dear Dr. Wasilenko:

I reviewed your letter dated December 20, 2021, and subsequent letters with additional information dated January 31, 2022, and February 4, 2022, related to your request for an exception to the regulatory requirement under 9 C.F.R. § 2.31(d)(1)(x), that limits an animal to one major operative procedure. You are making this request in order to continue the work performed under protocol #21-003 (approved 05/06/2021 and expires 05/06/2024), which will entail up to 6 caesarian sections on 5 adult female baboons (*Papio anubis*).

The subject animals are identified as numbers: 26741 (date of birth 6/1/2005), 26876 (date of birth 6/29/2005), 27320 (date of birth 10/24/2005), 07105 (date of birth 10/5/2005), and 03105 (date of birth 4/11/2005). Five of the 6 animals have already undergone at least 1 prior c-section, under protocols #15-009 (expired), #18-006 (expired) and #21-003 (current protocol). The subject animals are part of a single developmental study examining the role of estrogen (estradiol) on placental-fetal development and offspring function. (Further details of the methodology and rationale were provided in your communications noted above.)

After thorough review and consideration, the exception is **approved** from **June 15, 2022, to May 6, 2024,** with the following provisions that EVMS much ensure:

1. All work is performed in accordance with protocol #21-003.
2. This exception applies *only* to animals 26741, 26876, 27320, 07105 and 03105.
3. No more than 6 research-related major operative procedures are performed per animal per lifetime.
4. No animal undergoes a major operative procedure under this exception after May 6, 2024, without written approval from this office.
5. Adequate recordkeeping is maintained regarding the number of surgeries performed.
6. The IACUC evaluates animal well-being along with the effectiveness and soundness of methods and procedures, a minimum of every six months during the approval period.

Any failure to abide by the above provisions will result in the automatic withdraw of APHIS' approval of this exception. This approval is in accordance with 9 C.F.R. § 2.31(d)(1)(x)(C). If there are any questions, please contact your inspector, the Fort Collins office at (b) (6) or send inquiries to animalcare@usda.gov. Thank you.

Sincerely,

ELIZABETH GOLDENTYER

Digitally signed by ELIZABETH GOLDENTYER
Date: 2022.06.15 13:42:45 -04'00'

Betty Goldentyer, DVM
Deputy Administrator

USDA

United States Department of Agriculture
Animal and Plant Health Inspection Service

(b) (6)
INS-0000868299

Inspection Report

Eastern Virginia Medical School
358 Mowbray Arch, PO Box 1980
Norfolk, VA 23501

Customer ID: **497**
Certificate: **52-R-0003**
Site: 001
EASTERN VIRGINIA MEDICAL SCHOOL

Type: ROUTINE INSPECTION
Date: 02-MAY-2023

2.31(c)(7) **Repeat**

Institutional Animal Care and Use Committee (IACUC).

IACUC approval is not being secured prior to enacting significant changes in protocol #21-003 regarding the care and use of animals in ongoing activities.

**The protocol describes blood sampling for all animals on the pregnancy studies (adult female olive baboons) as being performed under ketamine sedation at 2-4 day intervals depending on the treatment group.

- In 2023, the daily treatment records for 17-year-old #07105 "Alissa" show that she underwent blood draws at daily intervals during multiple time periods. This includes, but is not limited to, daily blood draws during the following time periods: Jan 27th through January 30th, February 6th through Feb 11th, March 3rd through March 6th, 2023.
- In 2021, the daily treatment records for 16-year-old #26876 "Jemma" show that she underwent blood draws at daily intervals during multiple time periods. This includes, but is not limited to, daily blood draws during the following time periods: May 12th through 15th, May 17th through 20th, May 23rd through 30th, June 10th through 13th.

The protocol also indicates that no more than 10ml/kg of blood be collected from each animal over a month period, however the daily treatment records do not specify the volume of blood being drawn each day. Thus, there is no way to track and verify that the total volume does not exceed the upper limit approved by the IACUC. Increased blood draw

Prepared By: (b) (6)
Title:

Date: 03-MAY-2023

Received by Title: Facility Representative

Date: 03-MAY-2023

frequency and blood volume loss can have potential impacts on animal health and well-being and is a significant change to the current IACUC-approved protocol.

** The protocol states that all animals (adult female baboons) will be weighed monthly when they are on study. The protocol later states that animal weight is monitored weekly while the animal is on study when sedated. Records of 5 female baboons (ID #s: 26741, 26876, 27320, 07105, 03105) on the current protocol only have weights documented during their semi-annual physical and TB test, or during a surgical procedure. Upon request, no further documentation of animal weights during this study period could be provided by the facility. Monitoring the animal's weight weekly is described in the protocol as a clinical parameter to be monitored to indicate adverse effects, pain, and/or distress to the animals. Failing to follow the protocol and significantly decreasing the frequency of weigh-ins without IACUC approval does not allow the IACUC to review a change in the study procedure, especially one that is directly related to monitoring animal health and welfare.

** The protocol describes an anticipated adverse event ("seizures") in approximately 10% of animals receiving a study drug from days 100-170 gestation. Due to this known adverse event, the protocol documents steps that will be taken for animals found non-responsive, actively seizing, or unconscious which includes removing the animal from the cage, performing a blood gas analysis and glucose level, catheter placement and potential supplementation of dextrose depending on the blood glucose result. A 16-year-old female Olive Baboon #26876, "Jemma," while receiving the study drug, was found unresponsive at 6 am by a technician on June 16, 2021. There are no records indicating treatment was provided as outlined in the protocol. The only entry is from the attending veterinarian (AV) stating that she was found unresponsive at 6 am but by the time the AV arrived she had consumed some apples and was up and quiet, alert, and

responsive.

Failing to follow the protocol and significantly changing the procedures performed on animals without IACUC approval does not allow the IACUC to review and either approve, require modifications in, or deny the proposed changes. Correct by ensuring that the IACUC reviews and approves, requires modifications in (to secure approval), or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities.

This inspection and exit interview were conducted with facility representatives and the attending veterinarian.

Additional Inspectors:

(b) (6)

Prepared By: (b) (6)

Title:

Date: 03-MAY-2023

Received by Title: Facility Representative

Date: 03-MAY-2023

United States Department of Agriculture
Animal and Plant Health Inspection Service

Customer: 497
Inspection Date: 02-May-2023

Species Inspected

Cust No	Cert No	Site	Site Name	Inspection
497	52-R-0003	001	EASTERN VIRGINIA MEDICAL SCHOOL	02-MAY-2023

Count	Scientific Name	Common Name
000006	*Oryctolagus cuniculus*	DOMESTIC RABBIT / EUROPEAN RABBIT
000016	*Macaca fascicularis*	CRAB-EATING MACAQUE / CYNOMOLGUS MONKEY
000008	*Macaca mulatta*	RHESUS MACAQUE
000006	*Papio anubis*	OLIVE BABOON
000036	**Total**	

Animal and Plant Health Inspection Service

4700 River Road
Riverdale, MD 20737

USDA United States Department of Agriculture

May 16, 2023

William J. Wasilenko, Ph.D.
Vice Dean for Research and Institutional Official
EVMS Office of Research
735 Fairfax Avenue
Waitzer Hall, (b) (4)
Norfolk, Virginia 23507

Dear Dr. Wasilenko:

As you know, on June 15, 2022, APHIS approved an exception to the regulatory requirement under 9 C.F.R. § 2.31(d)(1)(x), that limits an animal to one major operative procedure from which it recovers, for 5 adult female baboons (*Papio anubis*) on Protocol #21-003. The approval letter stated that all activities must be performed in accordance with the protocol, and further stated that any failure to abide by the conditions in the letter would result in automatic withdrawal of APHIS' approval of this exception.

Following an inspection conducted on May 2, 2023, EVMS was cited under 9 C.F.R § 2.31(c)(7) for activities performed without IACUC approval prior to significant changes regarding the care and use of animals under protocol #21-003. As a result, and in accordance with 9 C.F.R. § 2.31(d)(1)(x)(C), APHIS hereby withdraws its approval of the exception for this protocol. No additional research-related major operative procedures from which they recover may be performed on animals 26741, 26876, 27320, 07105, and 03105.

If you have any questions, please contact your inspector, the Fort Collins office at (b) (6) (b) (6) or send inquiries to animalcare@usda.gov.

Sincerely,

ROXANNE MULLANEY

Digitally signed by ROXANNE MULLANEY
Date: 2023.05.16 13:55:42 -04'00'

Roxanne Mullaney, DVM
Acting Deputy Administrator

McCoy, Devora (NIH/OD) [E]

From: Morse, Brent (NIH/OD) [E]
Sent: Tuesday, May 23, 2023 9:53 AM
To: McCoy, Devora (NIH/OD) [E]
Cc: Tubbs, Jai (NIH/OD) [E]
Subject: FW: Eastern Virginia Medical School (OLAW case A3012-1J)
Attachments: 2022 MMOP EVMS Approval Letter 6-15-22 - signed.pdf; PST_Inspection_Report_Eastern_Virginia_Medical_School 5-2-23.pdf; EVMS MMOP Exception Withdrawal-signed.pdf

Follow Up Flag: Follow up
Flag Status: Completed

Hello Devora,

Please re-open this case 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: Divincenti, Louis - MRP-APHIS <Louis.Divincenti@usda.gov>
Sent: Tuesday, May 16, 2023 2:25 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Subject: [EXTERNAL] Eastern Virginia Medical School (OLAW case A3012-1J)

Hi Brent,

I think we sort of met on a conference call a few weeks ago. I've taken over for (b) (6) (b) (6) I'm writing to follow up on a situation that you had discussed with (b) (6) last year involving Eastern Virginia Medical School. To refresh your memory, inspectors found that the facility was conducting multiple major operative procedures (cesarean sections) in baboons without APHIS approval. As I understand, the work is funded by NIH. The institution was cited and subsequently granted an exception to the regulation.

A condition of that exception was that all activities had to be performed according to the protocol. Earlier this month, the facility was cited for performing activities on the protocol prior to IACUC approval of significant changes. I am attaching the inspection report for your information. Accordingly, we have decided to withdraw our approval of the exception, so the institution may not perform additional major recovery procedures on the 5 affected animals. I am also attaching both the approval letter and the withdrawal letter for your information.

I'm not sure what OLAW does from here, but wanted to make you aware since the work is funded through NIH and USDA has corresponded with you about previous noncompliance on this protocol. Please let me know if I can provide additional information.

Best wishes,

Louis

LOUIS DIVINCENTI, DVM, MS, DACLAM, DACAW | SENIOR VETERINARY MEDICAL OFFICER - RESEARCH
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