DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:
Office of Laboratory Animal Welfare
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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 24, 2020

Re: Animal Welfare Assurance
#A3245-01 (OLAW Case 4A]

Dr. Melur K. Ramasubramanian
Vice President for Research
Professor, Mechanical Engineering
University of Virginia
Box 400301
Charlottesville VA 22904-4301

Dear Dr. Ramasubramanian,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your August 18, 2020 letter reporting an adverse event with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Virginia. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the University of Virginia Animal Care and Use Committee (ACUC) determined that an adverse event occurred with respect to: the deaths of 5 mice in a biocontainment cage. The final report states 5 mice were housed in a biocontainment cage and found dead after being housed for a single day. It is stated the animals recently arrived to the facility and were in their acclimatization period. The Attending Veterinarian (AV) examined the animals and determined that suffocation occurred due to failure of the cage being docked completely on the biocontainment rack. After the AV questioned the vivarium supervisor and caretaker responsible for placing animals on the rack, they concluded the failure was due to the new biocontainment caging system. The AV further inspected the biocontainment caging system and discovered the following flaws with the caging system:

- A cage could be docked on the rack in a manner that fails to open all four ventilation valves and the yellow dot (indicator of improper placement on the rack) will not be completely visible and the alarm will not sound.

- The alarm system does not compensate for multiple cages with simultaneous failures wherein the alarm sounds and once a cage is addressed, the alarm does not sound if additional cages are improperly docked.

- The alarm can be programmed to be inactivated.

- After acknowledgement of the alarm, another alarm will not sound for an improperly docked cage unless the entire rack system is shut off and restarted.

The report states that all the racks purchased have the findings described above and that these discoveries are not described in the operator's manual. It is further stated that the manufacturer provided no on-site training to make special note of these findings. The manufacturer has been informed of these issues and provided detailed documentation. Since no alternative housing system is available in the biocontainment facility, the racks remain in use. Corrective actions implemented include the following:

- Retraining of the caretaker and research staff by the vivarium supervisor that work with the biocontainment cage system has occurred. Retraining summarized that caging must be very securely docked to preclude failure of ventilation of any cage.

- Signage has been posted in the biocontainment facility animal housing rooms demonstrating proper docking of cages and stresses that lack of a visible yellow dot does not indicate the cage has been properly docked on the rack.

It is noted that these animals were not supported by PHS funds. It is also noted that the IACUC reviewed the AV's letter detailing the event and found the actions of the AV to be appropriate and deemed no further action was necessary. This Office recommends the university continue to contact the manufacturer to address the concerns with the alarm system associated with the biocontainment rack.

Based on its assessment of this explanation, OLAW understands that the University of Virginia 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
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

A3245 -4A

University of Virginia
Serious Adverse Event Report
PHS Assurance # A3245-01

This document is a summary of the serious adverse event, actions taken, and final resolution. Due to the timing of the event, investigation, and resolution, a preliminary report was not submitted. The issue was not deemed a compliance issue by the IACUC.

UVA Case #: 2020-G

Nature of Event:	Condition that jeopardized the health and well-being of animals resulting in death (mice)
Summary of Event:	The Attending Veterinarian (AV) found and self-reported to the IACUC a serious adverse event resulting from a design flaw in newly purchased biocontainment caging. A single box containing five mice housed in biocontainment caging were found dead after having been housed in the space for a single day. The animals were newly arrived and were still in their acclimatization period had not been received any experimental manipulation. The Attending Veterinarian examined the animals and ascertained that the animals had suffocated due to a failure of the cage being docked or engaged completely into the biocontainment rack.
Action taken by Attending Veterinarian:	The AV interviewed both the vivarium supervisor and caretaker responsible for placing the animals into the biocontainment cage and rack, and they determined that the failure was due to the new biocontainment caging system. The AV further inspected the biocontainment caging system. When a biocontainment cage is properly docked into the rack, all check valves open and the cage is ventilated in a manner consistent with the health of the animals within the cage and containment of pathogenic microorganisms. If functioning as designed, an improperly docked cage presents a visible yellow dot on the rack and an alarm should be triggered within 10 seconds. The AV found the following problems: 1. A cage could be docked on the rack in a manner that fails to open all four ventilation valves and the yellow dot is not completely visible and the alarm does not sound. 2. The alarm system does not compensate for multiple cages with simultaneous failures wherein the alarm sounds and once one cage is addressed, the alarm does not sound if additional cages are in failure. 3. The alarm can be programmed to be inactivated; however, the operator may not be aware of this setting unless they move through several programming screens. 4. After the acknowledgment of an alarm, another alarm will not sound for an improperly docked cage unless the entire rack system is shut off and restarted.

	All of the racks purchased showed the same design flaws. The operator would not know these facts since they are not described in the operator's manual and the manufacturer provided no on-site training to point out these design flaws.
Management of Serious Adverse Event:	The AV informed the manufacturer's sales representative of these issues by email and within a detailed letter documenting the problems found.
Actions Taken to Prevent Future Occurrence of the Serious Adverse Event:	Having no alternative housing system in the biocontainment facility, the husbandry staff will continue to use the racks. The vivarium supervisor retrained the caretaker and research staff responsible for working with the biocontainment caging and racks. The retraining outlined that the caging must be very securely docked to preclude the failure of ventilation of any cage. Additionally, signage was posted in the biocontainment facility animal housing rooms where the new racks are located. The signage demonstrates proper docking of the cages and stresses that merely not seeing the yellow dot is insufficient demonstration of proper docking as an additional reminder.
Action Taken by IACUC:	At the next convened monthly meeting, the IACUC reviewed the letter sent by the AV describing the event and the serious adverse event report. The IACUC felt that the AV responded appropriately and no further action was deemed necessary.
Decision/Resolution:	The IACUC considered the incident resolved with no fault to the husbandry staff.
Federal Funding:	None
Notification of Final Disposition:	☒IO ☒OLAW

University of Virginia Institutional Official: (b) (6)

Melur K. Ramasubramanian

Walker, Keri (NIH/OD) [C]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, August 18, 2020 8:48 AM
To: Walker, Keri (NIH/OD) [C]
Subject: FW: UVA-OLAW Serious Adverse Event
Attachments: Serious Adverse Event REPORT 2020-G.pdf

Follow Up Flag: Follow up
Flag Status: Completed

From: Ramasubramanian, Melur K (mkr5a) <mkr5a@virginia.edu>
Sent: Monday, August 17, 2020 12:40 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6)
Subject: UVA-OLAW Serious Adverse Event

OLAW Division of Compliance Oversight,

Attached please find a "Serious Adverse Event Report". This problem came up quite recently and was referred to the IACUC very quickly. As a result, no preliminary report was filed.

The IACUC discussed this problem in some detail, and our attending veterinarian has contacted the manufacturer of this equipment to discuss these problems. We feel that we have trained our personnel to be alert for the special conditions which might not produce an alarm.

The IACUC considers this matter resolved and I concur. We can provide additional information about the specific equipment if you wish.

Regards,
Ram

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