Inspection Report

Ora, Inc
300 Brickstone Square
Andover, MA 01810

Customer ID: **507471**
Certificate: **14-R-0217**
Site: 001
ORA INC

Type: FOCUSED INSPECTION
Date: 27-APR-2022

2.31(c)(3)

Institutional Animal Care and Use Committee (IACUC).

From April 30 - May 5, 2021, there was a failure of the equipment that controls the light cycle in a housing room containing rabbits, resulting in continuous illumination for a week. Excessive illumination can have a variety of impacts on animal health and well being. Research facility staff also report instances of loss of temperature control in the vivarium.

These issues were not identified on subsequent semi-annual reports to the Institutional Official, which were prepared and submitted on June 11th, 2021, and January 5th, 2022. In order for the Institutional Official to be able to discharge their responsibilities under the AWA, semi-annual reports to the IO must contain a description of the nature and extent of a facility's adherence to this subchapter, must identify specifically any departures from provisions of this subchapter, and must state the reasons for any departure.

To be corrected by July 1st, 2022.

2.31(d)(1)(ii)

Institutional Animal Care and Use Committee (IACUC).

Prepared By: EILIS KARR
USDA, APHIS, Animal Care
Date: 04-MAY-2022

Title: VETERINARY MEDICAL OFFICER

Received by Title: IACUC Representative
Date: 04-MAY-2022

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Protocol #2020-06-13 contains a procedure description for intravitreal injections. Two amendments to add specific study compounds to be administered by intravitreal injection, A2 and AMD#3, had also been reviewed and approved by the IACUC. Neither the original protocol nor the amendments contain a written narrative description of the methods and sources used to determine that alternatives were not available for this procedure.

The IACUC shall determine that the principal investigator has considered alternatives to those procedures that may cause more than momentary pain or distress and that the principal investigator has provided a written narrative description of the methods and sources used to determine that alternatives were not available.

The IACUC must ensure that all protocols approved with potentially painful or distressful procedures are in compliance with this section. Correct by June 1st, 2022.

2.32(b)

Personnel qualifications.

The USDA inspector observed research staff conducting an unapproved procedure, directed by the principal investigator, on April 27, 2022. The principal investigator and research staff failed to follow the IACUC approved protocol when animals were observed in pain and distress on April 27, 2022. According to research and vivarium staff, they are uncertain of the methods whereby deficiencies in animal care and treatment are reported. The facility did not ensure that personnel involved in the animal care, treatment, and use were qualified to perform those activities.

Per this Section, it shall be the responsibility of a research facility to review personnel qualifications with sufficient frequency to fulfill the research facility's responsibilities under this section and 2.31.

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To be corrected by June 1st, 2022.

2.38(f)(1) **Critical**

Miscellaneous.

A study procedure on an IACUC approved protocol involves the use of specialized equipment on anesthetized rabbits in a darkroom. To conduct the procedure, an animal is placed on a platform and the device hood (which weighs approximately 5lb) is lowered to cover the animal's head. When the hood is lowered, there is a gap between the device hood and the platform through which the animal's neck and body extends. The specialized equipment, including the hood, is used to conduct studies on both rodents and rabbits. When in the fully closed position, the gap between the platform and the hood is approximately 1.5-2". The manufacturer of the equipment sells a device that adjusts the resting height of the hood to increase the gap by several inches to accommodate the larger body size of rabbits.

When this procedure was conducted on a cohort of 18 rabbits on July 13th, 2021, the equipment was not configured to accommodate rabbits. 3 rabbits died acutely and in sequence while being handled in the device. After these adverse events, the investigator continued the study on the remainder of the cohort.

Handling of all animals shall be done as carefully as possible in a manner that does not cause trauma, physical harm, or unnecessary discomfort.

The research facility voluntarily reported this incident on discovery and had instituted corrective measures at the time of this inspection, including the purchase and implementation of the device to adjust the equipment for rabbit use. To remain corrected from May 2nd, 2022.

Prepared By: EILIS KARR
USDA, APHIS, Animal Care
Date: 04-MAY-2022

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Date: 04-MAY-2022

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This is a continuation of the report for the focused inspection conducted April 27-28, 2022 and contains the remaining non-compliances found during the inspection.

This inspection was conducted with the Vivarium Manager and IACUC Chair on April 27-28, 2022. The exit interview were conducted with the Vivarium Manager, the IACUC Chair, and research staff on May 2, 2022.

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USDA, APHIS, Animal Care

Date: 04-MAY-2022

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Received by Title: IACUC Representative

Date: 04-MAY-2022

United States Department of Agriculture
Animal and Plant Health Inspection Service

Customer: 507471
Inspection Date: 27-Apr-2022

Species Inspected

Cust No	Cert No	Site	Site Name	Inspection
507471	14-R-0217	001	ORA INC	27-APR-2022

Count	Scientific Name	Common Name
000036	*Oryctolagus cuniculus*	DOMESTIC RABBIT / EUROPEAN RABBIT
000036	**Total**	

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2.31(c)(7) Direct

Institutional Animal Care and Use Committee (IACUC).

On April 27th, 2022, a study was initiated under IACUC protocol #2020-06-13 on 12 New Zealand rabbits involving the application of an experimental contact lens device to both eyes. The humane endpoints on the IACUC approved protocol state that if symptoms of ocular pain become so severe that the animal cannot open the eye and is reluctant to manually manipulating the eye to open, the animal will be euthanized. Research records and research staff indicate that 4 rabbits exhibited severe conjunctival swelling and redness. The research staff further report that the animals were so reluctant to open their eyes that general anesthetic was employed to restrain several animals for experimental observations. Per research staff, observations on this study are usually conducted on alert animals with brief manual restraint.

Failure of the research personnel to adhere to the humane endpoints in the IACUC approved protocol resulted in these animals experiencing unrelieved pain and distress and constitutes a significant change that was not reviewed or approved by the committee.

On April 27th during inspector review of an animal room containing rabbits, a research staff member was observed to administer eye drops (buffered salt solution, or BSS) to one rabbit. On discussion with the lab member, the PI had

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USDA, APHIS, Animal Care
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directed its administration to assess whether the solution was contributing to adverse reactions being observed in experimental animals. The use of BSS is approved on the protocol for lubrication of the eye throughout the contact lens study, but the experimental assessment of topically administered BSS in a naïve rabbit was not reviewed or approved by the IACUC. Changes in experimental design that include the addition of animal procedures and/or increase the number of animals used must undergo IACUC review and approval prior to being implemented.

Any proposed significant changes to ongoing activities must be reviewed by the IACUC and must be approved by the committee before the research activity is conducted.

To be corrected by May 2nd, 2022, or prior to the use of further animals on this protocol.

A focused inspection was conducted starting on April 27, 2022. This inspection report is limited to the Direct non-compliance identified during that inspection. An additional inspection report will be delivered with the other issues identified during this inspection.

This inspection was conducted April 27-28, 2022 and the exit briefing was conducted with the Vivarium Manager and IACUC Chair on April 28, 2022. A second exit briefing with additional facility representatives was conducted on May 2, 2022.

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000012	**Total**	