



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive – MSC 7982
Bethesda, Maryland 20892-7982
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

April 18, 2018

Re: Animal Welfare Assurance
#A3738-01 (OLAW Case R)

Dr. Michael Caulfield
President, Research Models & Services
Envigo
8520 Allison Pointe Blvd., (b) (4)
Indianapolis, Indiana 46250

Dear Dr. Caulfield,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 13, 2018 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Envigo RMS, following up on an initial report on March 26, 2018. According to the information provided, OLAW understands that several of 121 female mice shipped to a customer arrived pregnant and that 150 pups were born (and some died). This outcome constituted an unapproved significant change of the protocol. These mice had been injected with pristine for monoclonal antibody production but the technicians responsible were not trained to detect pregnant animals. The priming procedure had been transferred to another barrier without adequately planning animal inventory.

The immediate action taken upon discovery consisted of euthanizing the shipped adults and pups. The corrective actions consisted of retraining the technicians, improving animal identification, separating postpartum females into a holding cage, monitoring these females for possible pregnancy before injecting, and palpating the mice abdomens for pregnancy before injecting.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy.

Sincerely,

(b) (6)

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

cc: IACUC Contact



April 13, 2018

Brent C. Morse, DVM, DACLAM
Acting Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892-7982
E-mail: olawdco@mail.nih.gov

Dear Dr. Morse:

Re: Assurance# A3738-01 – Envigo RMS, Inc. (Envigo RMS)

As a follow up to our letter on March 26, 2018, regarding a protocol deviation, we are submitting this final report on the incident.

Under a Master Service Agreement, Envigo RMS provides a customer with postpartum female BALB/c mice that have been injected with pristane for monoclonal antibody production. Following delivery of this order, the customer notified Envigo RMS on March 22, 2018, that some of the female mice shipped were pregnant and had given birth at their facility or during transit. In total, 121 females and 150 pups were identified and euthanized following this discovery.

The Institutional Official, Attending Veterinarian, and the IACUC were notified of the event. A cross-functional team involving IACUC members, Quality Assurance, Management, and Senior Animal Technicians convened to determine root cause(s). The investigation determined:

- 1) The service for priming BALB/c mice with pristane had recently transferred from one Envigo RMS barrier to another without adequate inventory planning.
- 2) Technicians were not properly trained or had little experience in detecting possible pregnant animals prior to becoming injected with pristane.

To address these findings, the following corrective actions were implemented:

- 1) Extensive retraining of on-site technicians.
- 2) Improved identification and segregation of mice postpartum into a female only "holding cage."
- 3) Introduction of a mandatory "waiting period" for those female mice that may have contact with a male at any point after giving birth will be placed in the "holding cage." This allows for females with possible pregnancies to give birth prior to injection.
- 4) Addition of abdominal palpation to detect pregnancy prior to injection.

Senior Management, Quality Assurance, and the IACUC will continue to monitor the progress of these corrective actions.

Sincerely,

(b) (6)

Michael Caulfield
President and Institutional Official, Envigo RMS, Inc.

cc: Krishnan Kolappaswamy, DVM, PhD., Director and Attending Veterinarian, Envigo RMS, Inc.
Joseph F. Curlee, Jr., DVM, Chair, Envigo RMS IACUC

Envigo www.envigo.com

Gopee, Neera (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, April 17, 2018 10:39 AM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: Mike Caulfield; Krishnan Kolappaswamy; Buddy Curlee
Subject: RE: Final Report - Assurance A3738-01 - Envigo RMS, Inc.

Dear (b) (6)

Thank you for this final report. We will send an official response soon.

Best Regards,
Neera

Neera V. Gopee, DVM, PhD, DACLAM, DABT
Veterinary Medical Officer
Office of Laboratory Animal Welfare
National Institutes of Health

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From: (b) (6)@envigo.com]
Sent: Monday, April 16, 2018 2:26 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Mike Caulfield <mike.caulfield@envigo.com>; Krishnan Kolappaswamy <krishnan.kolappaswamy@envigo.com>; Buddy Curlee <buddy.curlee@envigo.com>
Subject: Final Report - Assurance A3738-01 - Envigo RMS, Inc.
Importance: High



Hello Dr. Morse,

Please see the attached final report for Assurance A3738-01 from Mike Caulfield, President and Institutional Official, Envigo RMS, Inc.

Thank you,

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A3738-R

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ENVIGO

Obtained by Rise for Animals.
Uploaded to Animal Research Laboratory Overview (ARLO) on 01/27/2021

March 26, 2018

Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892-7982
E-mail: olawdco@mail.nih.org

To Whom It May Concern:

Re: Assurance# A3738-01 – Envigo RMS, Inc.

In accordance with Assurance A3738-01 and PHS Policy IV.F.3 Envigo RMS, Inc. (Envigo RMS) provides this preliminary report of noncompliance regarding an incident of animal deaths and protocol deviation.

Envigo RMS provides postpartum female BALB/c mice that have been pristane-primed for monoclonal antibody production for a specific customer. It came to our attention on March 22, 2018, that some of these females shipped to the customers' facility on March 6, 2018, March 13, 2018, and March 20, 2018, were pregnant and gave birth shortly after delivery or during transit. In some instances the pups were dead. None of these animals were under PHS-funded contracts or grants.

The identified pregnant mice and pups will be euthanized. The shipment of any future orders to the customer has been suspended with immediate effect. An in-depth root cause analysis and corrective action plan will be implemented with the assistance of the IACUC and Quality Assurance.

A final report will be sent to the OLAW Office summarizing the root cause(s) and the corrective actions put in place to prevent future occurrences within 15 business days.

Sincerely,

(b) (6)

Michael Caulfield
President and Institutional Official, Envigo RMS, Inc.

cc: Krishnan Kolappaswamy, DVM, PhD, Director and Attending Veterinarian, RMS
Joseph F. Curlee, Jr., DVM, Chair, Envigo RMS IACUC

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, March 26, 2018 3:13 PM
To: IACUC Office; OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Preliminary Report - Assurance A3738-01 - Envigo RMS, Inc.

Thank you for this preliminary report. We are interested in the outcome of your analysis and your corrective action plan. We will open a case file and await your final report.

Regards, Brent Morse

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

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From: IACUC Office [mailto:IACUC.Office@envigo.com]
Sent: Monday, March 26, 2018 2:33 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: FW: Preliminary Report - Assurance A3738-01 - Envigo RMS, Inc.
Importance: High

Hello,

This email below returned to us as undeliverable. After checking the address, we are resending it. Please see the attached preliminary report regarding Assurance A3738-01 from Mike Caulfield, President and Institutional Official, Envigo RMS, Inc.

Thank you,

(b) (6)

From: IACUC Office
Sent: Monday, March 26, 2018 2:16 PM
To: 'olawdco@mail.nih.org' <olawdco@mail.nih.org>
Cc: Mike Caulfield <mike.caulfield@envigo.com>; Krishnan Kolappaswamy <krishnan.kolappaswamy@envigo.com>; Buddy Curlee <buddy.curlee@envigo.com>
Subject: Preliminary Report - Assurance A3738-01 - Envigo RMS, Inc.
Importance: High



To Whom It May Concern:

Please see the attached preliminary report regarding Assurance A3738-01 from Mike Caufield, President and Institutional Official, Envigo RMS, Inc.

Thank you,

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