OMB Number 0925-0765
Expiration Date: 11/30/2022

Annual Report to OLAW

Institution: Emory University
Assurance Number: A3180-01
Reporting Period: 10-01-2020 to 09-30-2021

This institution's Institutional Animal Care and Use Committee (IACUC), through the Institutional Official, provides this annual report to the Office of Laboratory Animal Welfare (OLAW).

I. Program Changes

[☐] A. There have been **no changes** in this institution's program for animal care and use as described in the Assurance.

[☒] B. Change(s) in this institution's program for animal care and use as described in the Assurance have occurred during this reporting period.

Select all that apply:

[☐] This institution's AAALAC accreditation status has changed (PHS Policy IV.A.2.).

[☐] AAALAC Accredited – Category 1

[☐] Non-Accredited – Category 2

[☒] This institution's program for animal care and use has changed (PHS Policy IV.A.1.a-i.). See Item VII [

[☐] The individual designated by this institution as the Institutional Official has changed.

[☒] The membership of this institution's IACUC has changed.

II. Semiannual Evaluations

This IACUC has conducted semiannual evaluations of the institution's program and inspections of the institution's facilities (including satellite facilities) on the dates below. Reports of the evaluations and inspections have been submitted to the Institutional Official. The reports include any IACUC-approved departures from the *Guide* with a reason for each departure, any deficiencies (significant or minor) that were identified, and a plan and schedule for correction of each deficiency.

A. Program Evaluations

Program	Review Date 1	Review Date 2
Bird Program 1	10/21/2020	4/7/2021
IACUC Program	10/21/2020	4/7/2021
Yerkes DAR Program	10/21/2020	5/5/2021^
Emory DAR Program	10/21/2020	4/7/2021
Bird Program 2	10/21/2020	4/21/2021
Mouse Program 1	10/21/2020	5/5/2021^

Mouse Program 2	10/21/2020	5/5/2021^
Mouse Program 3	10/21/2020	4/21/2021

^ 6 months plus up to 30-day extension as per OLAW guidance in NOT-OD-20-088

B. Facility Inspections

Facility	Previous Inspection Date	Inspection Date
(b) (4)	12/15/20	6/15/21
	1/21/21	7/15/2021
	2/16/21	9/17/21
	2/16/21	9/17/21
	1/26/21 1/28/21	7/27/21 7/29/21
	2/23/21 2/25/21	8/24/21 8/26/21
	3/11/21	9/9/21
	3/4/21 3/9/21	9/2/21 8/31/21
	3/25/21	9/23/21
	4/1/21	9/24/21

^ 6 months plus up to 30-day extension as per OLAW guidance in NOT-OD-20-088

III. Minority Views

[☐] A. There were **no minority** views during this reporting cycle.

[☒] B. Any minority views submitted by members of the IACUC regarding reports filed under PHS Policy IV.F. for this reporting cycle are attached.

IV. Signatures

IACUC Chairperson	**Institutional Official**
Name: Jeffrey Boatright, PhD	Name: Robert E. Nobles, DrPH, MPH, CIPA
Signature: (b) (6)	Signature: (b) (6)
Date: 11/17/2021	Date: 11/17/2021

V. Change in Institutional Official

Name:	
Title:	Degree/Credentials:
Name of Institution:	
Address: [*street, city, state, zip code*]	
Phone:	Fax:
E-mail:	

VI. Change in IACUC Membership

Institution: Emory University			
IACUC Contact Information			
Address: 1599 Clifton Road NE, 5th Floor 5.207 Atlanta, GA 30322			
E-mail: IACUC@emory.edu			
Phone: (b) (6)		Fax: (b) (6)	
IACUC Chairperson			
Name: Jeff Boatright, PhD			
Title: Professor		Degree/Credentials: PhD, FARVO	
PHS Policy Membership Requirements***: Scientist			
IACUC Roster			
Name of Member/ Code*	Degree/ Credentials	Position Title/ Occupational Background**	PHS Policy Membership Requirements***
S01 (Jeff Boatright)	PhD, FARVO	Professor	Scientist
V01 (Joyce Cohen)	VMD, DACLAM	Associate Director	Attending Vet (YNPRC)
V02 (Mike Huerkamp)	DVM, DACLAM	Director	Attending Vet (EU- DAR)
(b) (6)			Veterinarian
			Veterinarian
			Veterinarian
			Veterinarian
			Scientist
			Scientist
			Scientist
			Scientist

(b) (6)	
	Scientist
	Scientist
	Scientist
	Scientist
	Scientist
	Scientist
	Nonaffiliated
	Nonscientist
	Member (Unspecified Role)
	Unaffiliated
	Scientist Alternate for S01, S02, S03, S04, S05, S06, S07, S08, S09, S10, S11, S12
	Scientist Alternate for S01, S02, S03, S04, S05, S06, S07, S08, S09, S10, S11, S12
	Scientist Alternate for S01, S02, S03, S04, S05, S06, S07, S08, S09, S10, S11, S12
	Scientist Alternate for S01, S02, S03, S04, S05, S06, S07, S08, S09, S10, S11, S12
	Scientist Alternate for S01, S02, S03, S04, S05, S06, S07, S08, S09, S10, S11, S12
	Scientist Alternate for S01, S02, S03, S04, S05, S06, S07, S08, S09, S10, S11, S12
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V02, V05, V06
	Veterinary Alternate for V02, V05, V06
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V02, V05, V06

(b) (6)	
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V02, V05, V06
	Veterinary Alternate for V01, V03, V04
	Veterinary Alternate for V01, V03, V04
	Ex-officio, Non-voting
	Ex-officio, Non-voting
	Ex-officio, Non-voting
	Ex-officio, Non-voting
	Ex-officio, Non-voting
	Ex-officio, Non-voting
	Ex-officio, Non-voting
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	Ex-officio, Non-voting
	Ex-officio, Non-voting
	Ex-officio, Non-voting
	Ex-officio, Non-voting

* Names of members, other than the chairperson and veterinarian, may be represented by a number or symbol in this report to OLAW. Sufficient information to determine that all appointees are appropriately qualified must be provided and the identity of each member must be readily ascertainable by the institution and available to authorized OLAW or other PHS representatives upon request.	
** List specific position titles for all members, including nonaffiliated (e.g., banker, teacher, volunteer fireman; not "community member" or "retired").	
*** PHS Policy Membership Requirements:	
Veterinarian	veterinarian with training or experience in laboratory animal science and medicine or in the use of the species at the institution, who has direct or delegated program authority and responsibility for activities involving animals at the institution.
Scientist	practicing scientist experienced in research involving animals.
Nonscientist	member whose primary concerns are in a nonscientific area (e.g., ethicist, lawyer, member of the clergy).
Nonaffiliated	individual who is not affiliated with the institution in any way other than as a member of the IACUC and is not a member of the immediate family of a person who is affiliated with the institution. This member is expected to represent general community interests in the proper care and use of animals and should not be a laboratory animal user or former user. A consulting veterinarian may not be considered nonaffiliated.

Statement of Burden

Public reporting burden for this collection of information is estimated to average 90 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0765). Do not return the completed form to this address.

VII: Change(s) in this institution's program for animal care and use

- Emory University Division of Animal Resources led by Dr. Michael Huerkamp discontinued the services of an additional veterinarian hired during the 2020 reporting period.
- As indicated above, the IACUC used guidance from NOT-OD-20-088 to delay some site inspections from the required 6 months to add up to an additional 30 days. These are noted in the tables for site inspections. All other inspections were completed within the 6-month window.
- Emory University currently has two NASA funded research projects. Neither of these projects involve use of the International Space Station.
- Due to the COVID-19 pandemic, the IACUC is conducting IACUC business by telecommunications via Zoom. IACUC business includes full committee review meetings, semiannual site inspections, and training of members.

EMORY UNIVERSITY | Division of Animal Resources
Emory Integrated Core Facilities

MINORITY VIEW OF THE ATTENDING VETERINARIAN (AV)
July 28, 2021

RE: **Mandy Ford** PROTO201700378 "Memory T cells and sepsis-induced immune dysregulation"
Craig Coopersmith PROTO201700361 "Mechanisms of Sepsis"

Executive Summary: This minority view is in opposition to recent IACUC approval of the protocols listed above allowing intratracheal injection via a surgical approach to introduce bacteria into the lungs for purposes of inducing pneumonia when a viable, more humane, validated, long-standing, and pathophysiologically relevant alternative exists. The alternative for substance administration into the lungs is orotracheal intubation. The AV is of the professional opinion that actual harm could be reduced in relation to the potential benefit of these studies and was not.

Orotracheal Intubation offers the following advantages:

1) It is non-invasive not resulting in tissue disruption or leaving behind a trail of surgical and puncture site inflammation and thus is more humane.
2) It is the same procedure of inserting a tube into the trachea as that to maintain inhalation anesthesia.
3) It is pathophysiologically-relevant making use of the natural route for conveyance of bacteria into the lungs to cause bronchopneumonia.
4) It is expedient in the hands of skilled operators.
5) It eliminates the time necessary to shave skin, aseptically prep the surgical site, close an incision, or lose mice from the experiment due to infection at the incision site.
6) It requires no surgical instruments to maintain, sterilize or manage in and out of a biocontainment area.
7) The use of peri-operative analgesics is eliminated as a variable associated with the model.
8) DAR has the skill within the training unit to teach the method to willing learners.
9) Non-invasive pulmonary instillation is established in research, including induction of bacterial pneumonia. For example:
    - "Imaging of bioluminescent *Klebsiella pneumoniae* induced pulmonary infection in an immunosuppressed mouse model", 2020.
        - AV Note: In a dose-dependent manner, orotracheal intubation reliably resulted in instillation of *Klebsiella* to the lungs, proliferation of the pathogen there, and infection confined to the lungs as confirmed by bacterial bioluminescence.
        - Citation: doi:10.1177/0300060520956473
    - "Methodology for the measurement of mucociliary function in the mouse by scintigraphy", 2001
        - AV note: One finding was the reliable deposition of radiolabeled particles into the lungs via orotracheal intubation.
        - Citation: https://doi.org/10.1152/jappl.2001.90.3.1111
    - "Pneumonia models and innate immunity to respiratory bacterial pathogens", 2005.
        - AV Note: In this review paper, the authors advocate induction of pneumonia by direct administration of bacteria into the trachea via oropharyngeal catheter or into the nose of anaesthetized animals.
        - Citation: DOI: 10.1097/01.shk.0000191385.41689.f3

Michael J. Huerkamp, DVM, DACLAM
Executive Director, Division of Animal Resources
Whitehead Biomedical Research Building
615 Michael Street - (b) (4)
Atlanta, Georgia 30322

- "Cystic fibrosis lung disease following infection with *Pseudomonas aeruginosa* in Cftr knockout mice using novel non-invasive direct pulmonary infection technique", 2005.
  - AV Note: The study relied upon the method of instillation of bacteria into the lungs by tracheal intubation.
  - Citation: https://doi.org/10.1258/0023677054306944
- "Susceptibility of irradiated B6D2F1/J mice to Klebsiella pneumoniae administered intratracheally: A pulmonary infection model in an immunocompromised host", 2003
  - AV note: Orotracheal intubation was the means used to induce pneumonia for these studies to evaluate therapies.
  - Citation: PMID: 14524416
- "An improved simple method of mouse lung intubation", 2009
  - AV Note: This was a descriptive paper describing how to simply use the intubation procedure.
  - Citation: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4587594/

Disclaimer: These citations are not representative of an exhaustive literature search, but merely are provided to buttress the fact that the alternative advocated by the AV has a history of successful use including in association with murine pneumonia and sepsis models.

The Argument that Intratracheal Injection Prevents Contamination of the Oral Cavity, Risk of Subsequent Ingestion of Some Bacteria, and Significant Alteration of the Microbiome.

The investigators contended, and the IACUC accepted, that there were risks of residual bacterial inoculum, intended for the lungs, dripping from the catheter during extubation and thus at risk of the swallowing of bacteria into the gastrointestinal (GI) tract to the detriment of the GI microbiome. Based upon this theoretical concern, the investigators were of the belief they could not even try orotracheal instillation as an alternative. One fear was that the integrity of the alternative advocated by the AV required substantiation using radiolabeled agent to ensure delivery of agent solely into the lungs, and not diversion into the GIT. While the conversation related to this argument suffered from insufficient time when the investigators and DAR vets broached the topic on July 7, 2021, the AV does not follow the logic of the risk.

(1) First, subsequent review of the literature, suggests the orotracheal means of inoculation has been validated and proven in the manner desired:
   - "Imaging of bioluminescent *Klebsiella pneumoniae* induced pulmonary infection in an immunosuppressed mouse model", 2020. Citation: doi:10.1177/0300060520956473
   - "Methodology for the measurement of mucociliary function in the mouse by scintigraphy", 2001. Citation: https://doi.org/10.1152/jappl.2001.90.3.1111

(2) The AV questions whether the procedure preferred by the investigators and allowed by the IACUC, intratracheal injection by surgical approach, has been tested and validated in an equivalent manner as was asked for the non-surgical alternative?

(3) While it is possible there may be Inadvertent ingestion of some bacteria following extubation…
   a. Any amount of inoculum swallowed would be in *de Minimis* amounts and arguably inconsequential.
   b. These studies are conducted with mice residing in colonies where *Klebsiella* is not excluded and may be enzootic to varying degrees in the GI tract and oropharynx of colony mice.

c. Mice engage in coprophagy and thus may cross-inoculate each other with resident coliforms, including *Klebsiella*.

(4) The scientific aims of the two protocols do not obviously address dynamics of the GI microbiome as a variable to be investigated in conjunction with pneumonia models, although there may be intrinsic possibilities, thus making it difficult for the AV to appreciate the ultimateconcern:

a. Mandy Ford PROTO201700378 "Memory T cells and sepsis-induced immune dysregulation"
   - Aim 1: Determine the mechanisms by which T cell cosignaling molecules contribute to immune dysregulation during sepsis
   - Aim 2: Determine the role of T cell cosignaling molecules on memory T cells and secondary effectors during sepsis

b. Craig Coopersmith PROTO201700361 "Mechanisms of Sepsis"
   - Determine potential mechanisms through which cancer increases mortality in septic mice.
   - Determine whether prevention of lymphocyte apoptosis worsens survival in septic mice with cancer and mechanisms responsible for this.
   - Determine whether restoring gut integrity improves survival in septic mice with cancer and mechanisms responsible for this.
   - Determine the mechanisms by which TIGIT blockade improves sepsis survival in hosts with preexisting malignancy.
   - Interrogate the pathogenicity of two CD4+ T cell subsets upregulated in the setting of cancer sepsis: PD-1hi vs. 2B4+ BTLA+ LAG-3+.
   - Identify the role of IL-27 in establishing T cell dysregulation in the setting of cancer and sepsis.
   - Determine mechanisms through which the immune system and microbiome alter survival in mice lacking the TJ-associated protein junctional adhesion molecule-A (JAM-A).
   - Determine mechanisms and functional significance of altering the leak pathway and pore pathway of intestinal permeability in sepsis.
   - Determine mechanisms mediating decreased intestinal migration in sepsis.
   - Determine mechanisms through which the combination of chronic alcohol ingestion and sepsis worsens gut permeability.
   - Determine the mechanisms underlying the ability of CTLA-4 blockade to decrease mortality during sepsis in the setting of chronic alcohol ingestion.
   - Determine the role of CD43 in increasing sepsis-induced mortality in the setting of chronic alcohol exposure.

Please ensure that this minority view is included in the semi-annual report record for this period and in the annual report to OLAW for the year. If that is not possible, please inform me so that I can send the view directly to OLAW.

Sincerely,

(b) (6)

Michael J. Huerkamp, DVM, DACLAM
Attending Veterinarian
Professor, Pathology and Laboratory Medicine

"...it is widely recognized that the humanist possible treatment of experimental animals, far from being an obstacle, is actually a prerequisite for successful animal experiment."

~W.M.S. Russell and R.L. Burch~

1959