

60th Medical Group (AMC), Travis AFB, CA
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)
FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20170019A

DATE: 1 March 2018

PROTOCOL TITLE: Development and Validation of a Porcine (*Sus scrofa*) Sepsis Model.

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Dr. Guillaume Hoareau

DEPARTMENT: SGSE

PHONE #: 215-275-0395

INITIAL APPROVAL DATE: 27 April 2017

LAST TRIENNIAL REVISION DATE: N/A

FUNDING SOURCE: SG

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
<i>Sus scrofa</i>	10	3	7

2. PROTOCOL TYPE / CHARACTERISTICS: (Check all applicable terms in **EACH** column)

☐ Training: Live Animal	☐ Medical Readiness	☐ Prolonged Restraint
☐ Training: non-Live Animal	☐ Health Promotion	☐ Multiple Survival Surgery
☐ Research: Survival (chronic)	☐ Prevention	☐ Behavioral Study
☒ Research: non-Survival (acute)	☐ Utilization Mgt.	☐ Adjuvant Use
☐ Other ()	☐ Other (Treatment)	☐ Biohazard

3. PROTOCOL PAIN CATEGORY (USDA): (Check applicable) ☐ C ☒ D ☐ E

4. PROTOCOL STATUS:

***Request Protocol Closure:**

☐ Inactive, protocol never initiated

☐ Inactive, protocol initiated but has not/will not be completed

☒ Completed, all approved procedures/animal uses have been completed

5. Previous Amendments:

List all amendments made to the protocol. **IF none occurred, state NONE. Do not use N/A.**

For the Entire Study Chronologically

Amendment Number	Date of Approval	Summary of the Change
1	3 Aug 17	Personnel

6. FUNDING STATUS: Funding allocated: \$18,690.00

Funds remaining: \$ 0.00

7. PROTOCOL PERSONNEL CHANGES:

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? X Yes No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

<u>NAME</u>	<u>PROTOCOL FUNCTION</u>	<u>IACUC APPROVAL</u>
Capt Carl Beyer	AI	Yes
Capt Harris Kashtan	AI	Yes
Capt Andrew Wishy	AI	Yes

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

<u>NAME</u>	<u>PROTOCOL FUNCTION</u>	<u>DATE OF DELETION</u>
Lt Col Timothy Williams	AI	3 August 2017
Maj Erik DeSoucy	AI	3 August 2017
Capt Meryl Simon-Logan	AI	3 August 2017
Capt Emily Tibbits	AI	3 August 2017

8. PROBLEMS / ADVERSE EVENTS: Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

No unanticipated complication was encountered.

9. REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

None.

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

None.

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

None

10. PUBLICATIONS / PRESENTATIONS: (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

None.

11. PROTOCOL OBJECTIVES: (Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?)

This protocol demonstrated physiologic responses of lipopolysaccharide injection to pigs to induce a state of sepsis. We showed that this model was not reproducible and induced a wide range of cardiovascular responses that would not be suitable for future research.

12. PROTOCOL OUTCOME SUMMARY: (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

Objectives: We sought to develop and validate a porcine model of a sepsis-like state suitable for the future study of EPACC in sepsis. Specifically, we aimed at determining the proper LPS loading dose and constant rate infusion regimen to achieve a sepsis-like state.

Materials and methods: Animals were anesthetized and instrumented for cardiovascular monitoring. Lipopolysaccharide (LPS, a large molecule present on the outer layer of Gram negative bacteria) (Sigma Aldrich, ready-made solution, L5293) was injected at various dosing regimen (with or without loading dose). Animals' cardiovascular parameters (heart rate, mean arterial blood pressure) were monitored continuously.

Results: We observed that animals had unpredictable responses to LPS injection and could not identify a protocol that would be reproducible. For a given dose we would observe some pigs displaying little to no response while others may suffer decompensated vasodilatory shock leading to death.

Conclusions/applications: LPS injection is not a suitable model for our research effort. We are currently validating a live bacteria infusion protocol to induce sepsis in pigs.

GUILLAUME L. HOAREAU, DVM, PhD

(Date)

Attachments:

Attachment 1: Defense Technical Information Center (DTIC) Abstract Submission **(Mandatory)**

Attachment 1

Defense Technical Information Center (DTIC) Abstract Submission

This abstract requires a brief (no more than 200 words) factual summary of the most significant information in the following format: Objectives, Methods, Results, and Conclusion.

Objectives: We sought to develop and validate a porcine model of a sepsis-like state suitable for the future study of EPACC in sepsis. Specifically, we aimed at determining the proper LPS loading dose and constant rate infusion regimen to achieve a sepsis-like state.

Methods: Animals were anesthetized and instrumented for cardiovascular monitoring. Lipopolysaccharide (LPS, a large molecule present on the outer layer of Gram negative bacteria) (Sigma Aldrich, ready-made solution, L5293) was injected at various dosing regimen (with or without loading dose). Animals' cardiovascular parameters (heart rate, mean arterial blood pressure) were monitored continuously.

Results: We observed that animals had unpredictable responses to LPS injection and could not identify a protocol that would be reproducible. For a given dose we would observe some pigs displaying little to no response while others may suffer decompensated vasodilatory shock leading to death.

Conclusion: LPS injection is not a suitable model for our research effort. We are currently validating a live bacteria infusion protocol to induce sepsis in pigs.

Grant Number: _____

From: _____

****If you utilized an external grant, please provide Grant # and where the grant came from. Thank you.**