AWARD NUMBER: W81XWH-22-1-1109

TITLE: Intraosseous Antibiotic for Point-of-Care Wound Prophylaxis

PRINCIPAL INVESTIGATOR: Jessica C Rivera, MD, PhD

CONTRACTING ORGANIZATION: Louisiana State University Health Sciences Center
New Orleans, LA

REPORT DATE: October 2023

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
October 2023	Annual	30Sep2022-29Sep2023

4. TITLE AND SUBTITLE

Intraosseous Antibiotic for Point-of-Care Wound Prophylaxis

5a. CONTRACT NUMBER
W81XWH-22-1-1109

5b. GRANT NUMBER
OR210117

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Jessica C Rivera, MD

E-Mail: jrive5@lsuhsc.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

LSU Health Sciences Center – New Orleans
433 Bolivar Street
New Orleans, LA 70112-7021

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Combat extremity wounds are severe wounds that often involve multiple tissues and carry the risk of infection. This applied research will leverage skills and techniques already critical to tactical combat casualty care training including the intraosseous catheter placement for the delivery of antibiotic to protect composite tissue wounds from infection even with concomitant use of an extremity tourniquet which may compromise tissue antibiotic concentration distal to the tourniquet. A large animal contaminated, composite tissue model will be used to test if antibiotics delivered by intraossesous catheter will be more effective than standard IV antibiotic delivery for decontaminating wounds. We hypothesize intraosseous antibiotic administration would offer infectious wound protection following severe extremity injury for limb with and without concomitant tourniquet use.

15. SUBJECT TERMS
Musculoskeletal System; Injury; Infectious Diseases & Agents

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified	20	USAMRDC

TABLE OF CONTENTS

1. INTRODUCTION:

Combat extremity wounds are severe wounds that often involve multiple tissues and carry the risk of infection. This applied research will leverage skills and techniques already critical to tactical combat casualty care training including the intraosseous catheter placement for the delivery of antibiotic to protect composite tissue wounds from infection even with concomitant use of an extremity tourniquet which may compromise tissue antibiotic concentration distal to the tourniquet. A large animal contaminated, composite tissue model will be used to test if antibiotics delivered by intraossesous catheter will be more effective than standard IV antibiotic delivery for decontaminating wounds. We hypothesize intraosseous antibiotic administration would offer infectious wound protection following severe extremity injury for limb with and without concomitant tourniquet use.

2. KEYWORDS: *Provide a brief list of keywords (limit to 20 words).*

Extremity injury; wounds; wound protection; infection; infection prophylaxis; prolonged field care; intraosseous; antibiotics

3. ACCOMPLISHMENTS: *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Major Task 1: Regulatory Approvals—Local IACUC and ACURO approvals have been completed. We initially anticipated this process to take 6 months and to have begun Task 3 at the 6 month mark.

Major Task 2-5: Animals surgeries—not yet begun

Major Task 6-7: Sample analysis, dissemination—not yet begun

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include

pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Local IACUC, local Biosafety Committee, and ACURO approvals have been completed. These are all the regulatory requirements for study initiation.

In the meantime, we have secured a MolecuLight device which will be used to perform the bioburden imaging on the model wounds. We have been optimizing the protocol for the MolecuLight imaging on a mouse model using the planned fluorescent bacteria (Xen36 Staph aureus). The bacteria have been expanded in culture and found to be retaining fluorescence.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these

project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Now that we have all regulatory requirements complete, the first animal surgeries are scheduled in November 2023. While we will still plan to begin with 2 animals to assure the protocol runs smoothly, follow on surgery dates will quickly be underway.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

The local IACUC protocol was delayed. Our vivarium has recently undergone several expansions/upgrades which is positive. However, planning a large animal study during this time was a challenge as many of the items pertinent to the IACUC protocol details were not clear during this transition.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

During the remodeling and renovation of the animal care facilities, new large animal protocols could not be accommodated. Because many details such as housing, procedure rooms, and post operative protocols are necessary for the IACUC protocol, this transition did delay the protocol. Now that this step is completed (and our facilities are improved) we do not have other anticipated problems.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Because of the above, spending for the first year has been less than anticipated. We anticipate as animals surgeries are caught up in the next year that expenditures originally anticipated in year 1 will be needed as expected in year 2.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or

equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Not applicable

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

) **Publications, conference papers, and presentations**
Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report

Website(s) or other Internet site(s)

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name:	Jessica Rivera
Project Role:	PI
ORCID:	
Nearest person month worked:	0.2
Contribution to Project:	Completed IACUC, IBC, and ACURO protocols; worked on luminescent bacteria imaging optimization in a small animal model

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
<u>Organization Name:</u>
<u>Location of Organization: (if foreign location list country)</u>
<u>Partner's contribution to the project</u> (identify one or more)

- ⁾ *Financial support;*
- ⁾ *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- ⁾ *Facilities (e.g., project staff use the partner's facilities for project activities);*
- ⁾ *Collaboration (e.g., partner's staff work with project staff on the project);*
- ⁾ *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- ⁾ *Other.*

Not applicable

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ebrap.org/eBRAP/public/index.htm*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil/Pages/Resources.aspx) should be updated and submitted with attachments.*

9. APPENDICES:

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Appendix document 1: IACUC approval
Appendix document 2: IBC approval
Appendix document 3: ACURO approval

PROTOCOLS

kuali

LSU Health NEW ORLEANS
INSTITUTIONAL ANIMAL CARE & USE COMMITTEE

IACUC Certificate of Determination

From: LSUHSC-NO Institutional Animal Care & Use Committee

To: Rivera, Jessica

Date: Monday, May 15th 2023

Re: Protocol #4230, Intraosseous Antibiotics for Point of Injury Wound Prophylaxis

The LSUHSC-NO IACUC has reviewed and approved the **Initial** application of the above-referenced protocol. In the judgment of the IACUC, the procedures delineated in this application conform to the pertinent federal rules and regulations regarding use and care of animals. The IACUC made the following determinations:

IACUC Review Action: APPROVAL

Protocol Version: 3

Effective Date: Monday, May 15th 2023

Protocol Expiration Date: Friday, May 15th 2026

Approval comments (if any) to note:

Approved attachments associated with the submission (if any) include:

, , , ,

As the Principal Investigator, you are responsible for complying with, and assuring all study staff comply with, all federal regulations and IACUC policies and procedures, including post-approval study requirements, pertaining to animal research. IACUC policies and procedures, post-approval study requirements, and other information are available at the **LSUHSC IACUC website**.

Please note: *Per federal regulations and institutional policy, this protocol is approved for a maximum of 3 years. To continue the research beyond the expiration date, you must submit and receive approval of a new IACUC application. All future modifications to the protocol, including change in personnel, must be reviewed and approved by the IACUC prior to implementation.*

PROTOCOLS

kuali

LSU Health NEW ORLEANS
INSTITUTIONAL BIOSAFETY COMMITTEE

IBC Certificate of Determination

From: LSUHSC-NO Institutional Biosafety Committee

To: Rivera, Jessica

Date: Thursday, February 9th 2023

Re: Protocol #4741, Intraosseous Antibiotics for Point of Injury Wound Prophylaxis

The LSUHSC-NO IBC has reviewed and approved the **Initial** application of the above-referenced protocol. In the judgment of the IBC, the procedures and safety practices delineated in this application conform to the pertinent federal rules and regulations as outlined in the *NIH Guidelines*. The IBC made the following determinations:

IBC Review Action: APPROVAL

Protocol Version: 2

Effective Date: Thursday, February 9th 2023

Annual Continuing Review Date: Friday, February 9th 2024

Protocol Expiration Date: Wednesday, February 9th 2028

Approval comments (if any) to note:

Good luck doctora

Approved attachments associated with the submission (if any) include:

As the Principal Investigator, you are responsible for complying with, and assuring all study staff comply with, all federal regulations and IBC policies and procedures, including post-approval study

requirements, pertaining to this research project. IBC policies and procedures, post-approval study requirements, and other information are available at the **LSUHSC IBC website**.

Please note: *Per federal regulations and institutional policy, this protocol is approved for a maximum of 5 years but still requires annual continuing review. Please pay careful attention to email notifications regarding continuing reviews (sent starting 30 days prior to the continuing review deadline) and submit a Renewal application in sufficient time for review and approval by the next annual review deadline, Friday, February 9th 2024. To continue the research beyond the expiration date, you must submit and receive approval for a new IBC application. All future modifications to the protocol, including change in personnel, must be reviewed and approved by the IBC prior to implementation.*

DEPARTMENT OF THE ARMY

HEADQUARTERS, U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
810 SCHREIDER STREET
FORT DETRICK, MD 21702-5000
July 17, 2023

Director, Office of Human and Animal Research Oversight
Animal Care and Use Review Office (ACURO)

Subject: Approval of Proposal Number OR210117, Award Number W81XWH-22-1-1109 entitled, "Intraosseous Antibiotic for Point-of-Care Wound Prophylaxis"

Jessica C. Rivera
Louisiana State University Health Sciences Center
Shreveport, LA, US

Dear Jessica Rivera:

Reference: (a) DOD Instruction 3216.01, "Use of Animals in DOD Conducted and Supported Research and Training"
(b) US Army Regulation 40-33, "The Care and Use of Laboratory Animals in DOD Programs"

In accordance with the above references, ACURO protocol OR210117.e001 entitled, "Intraosseous Antibiotics for Point of Injury Wound Prophylaxis," IACUC protocol number 4230, Protocol Principal Investigator Dr. Jessica C. Rivera, is approved by ACURO as of 07/17/2023 for the use of pigs and will remain so until modification, expiration or cancellation. This protocol was approved by the Louisiana State University Health Sciences Center IACUC on 05/15/2023; IACUC approval expires 05/15/2026.

Required Actions:

A. Submit to ACURO for review and approval prior to implementing:

- IACUC-approved de novo reviews of the protocol
- IACUC-approved significant changes to this protocol (see guidance document)

B. Notify ACURO within 5 business days of any of the following:

- Any noncompliance, suspensions or adverse events (see guidance document)
- Receipt of notification that the institution is under investigation by USDA
- AAALAC, International accreditation status change

For further assistance, please contact ACURO at (301) 619-6694, FAX (301) 619-4165, or via e-mail: usarmy.detrick.medcom-usamrmc.other.acuro@health.mil.

NOTE: Do not construe this correspondence as approval for any contract funding. Only the Contracting Officer or Grant Officer can authorize expenditure of funds. It is recommended that you contact the appropriate Contract Specialist or Contracting Officer regarding the expenditure of funds for your project.

Sincerely,

Krinon Moccia, DVM, MPH, DACLAM
LTC, VC, USA
Director, Animal Care and Use
Review Office

Copies Furnished:
Sven Oertel
Charles Steadman
Adam Caro
Dr. Jessica C. Rivera
Dr. Kenneth Furdella
Dr. Prem Yadav
Ann Clesi