Pilot Study: Ketamine for acute pain after rattlesnake envenomation

Study Protocol and Statistical Analysis Plan

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THE UNIVERSITY OF ARIZONA Research Innovation & Impact

IRB Protocol for Human Subjects Research

Basic Information	
Title of Study:	Pilot Study: Ketamine for acute pain after rattlesnake envenomation
Short Title:	Ketamine Pilot Study
Principal Investigator Name:	Meghan Spyres, MD
Principal Investigator's Department/Unit:	Toxicology

1.0 Background (Limit 1,000 words):

Provide the scientific or scholarly background for the proposed Human Research. Discuss relevant prior experience or preliminary data (e.g., existing literature).

Multiple studies have shown ketamine to be safe and effective agent for acute pain syndromes [1,2,3]. Rattlesnake envenomations classically result in severe pain that can be difficult to control, despite use of opioids, non-opioid analgesics, and positioning techniques, including splinting and elevation. Furthermore, the ongoing opioid epidemic pushes clinicians to explore non-opioid agents to avoid unnecessary exposure of patients to these high-risk medications. At least one small study has shown ketamine to be safe in rattlesnake envenomated patients.

REFERENCES

1. Karlow N, et al. A systematic review and meta-analysis of ketamine as an alternative to opioids for acute pain in the emergency department. Acad Emerg Med. 2018 Oct;25(10):1086-1097. doi: 10.1111/acem.13502. Epub 2018 Jul 17. PMID: 30019434.

2. Brandehoff N, Benjamin JM, Balde C, Chippaux JP. Ketamine for pain control of snake envenomation in Guinea: A case series. Toxicon. 2020 Nov;187:82-85. doi: 10.1016/j.toxicon.2020.08.020. Epub 2020 Sep 3. PMID: 32891662.

3. Balzer N, McLeod SL, Walsh C, Grewal K. Low-dose Ketamine For Acute Pain Control in the Emergency Department: A Systematic Review and Meta-analysis. Acad Emerg Med. 2021 Apr;28(4):444-454. doi: 10.1111/acem.14159. Epub 2021 Jan 2. PMID: 33098707.

4. Andolfatto G, Willman E, Joo D, Miller P, Wong WB, Koehn M, Dobson R, Angus E, Moadebi S. Intranasal ketamine for analgesia in the emergency department: a prospective observational series. Acad Emerg Med. 2013 Oct;20(10):1050-4. doi: 10.1111/acem.12229. PMID: 24127709.

5. Gallagher EJ, et al. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. Ann Emerg Med December 2001;38:633–8, and Bird SB,

Dickson EW. Clinically significant changes in pain along the visual analog scale. *Ann Emerg Med*. December 2001;38:639–43.

2.0 Lay Summary:

Provide a brief description of the proposed research using terms that someone who is not familiar with the science or discipline can understand.

This is a pilot study to evaluate pain responses from two different approved medications (ketamine and fentanyl) in the treatment of pain after rattlesnake envenomation (RSE). Both medications are currently used in standard practice to treat both acute and chronic pain and are options for pain management after RSE. Multiple studies exist showing ketamine to be both safe and effective for the treatment of acute pain, and to be as good as or better than opioids for this indication. The specific comparison of ketamine to fentanyl, however, has never been studied for the treatment of acute pain after rattlesnake envenomation in the United States. We plan to measure pain scores after a single dose of ketamine or fentanyl in patients shortly after being envenomated, followed by continued treatment of pain guided by the treating doctor. There will be no restrictions on additional pain medications given and no other changes to the treatment of these patients during their hospitalization. This research is important because pain after RSE can be difficult to control and may require frequent, high doses of opioids for several days. An effective non-opioid medication would be helpful both to better-control pain and to reduce exposure to opioids in this patient population. This study will compare patient-reported pain scores after receiving a single dose of ketamine or fentanyl in patients with rattlesnake bites who have been admitted to the toxicology service at Banner – University Medical Center Phoenix (BUMCP).

3.0 Purpose:

Describe the purpose, specific aims, objectives, questions to be answered, hypotheses, and/or primary and secondary study endpoints of the Human Research.

The purpose of this study is to evaluate differences in pain levels following a single administration of fentanyl or ketamine to treat pain after rattlesnake envenomation. The aim is to assess pain scores prior to medication administration, then 15, 30, 60, and 120 minutes after single medication administration. Primary endpoint is pain score at 30 minutes after medication administration. Secondary endpoints are pain scores at additional time points, need for rescue medication, adverse medication effects, and patient pain satisfaction scores at discharge.

Primary hypothesis

There will be no difference in pain responses in the two groups.

Fentanyl and ketamine are commercially available and used as FDA approved for the management of pain in the United States.

4.0 Funding Information:

Indicate all sources of funding for the project, including gift funds, departmental funds, or other internal funding. For each funder, list the name of the funder, and the institutional proposal number or award number you received from Sponsored Projects. For externally funded projects, the information below should match the Study Funding Sources in eIRB.

☒ **No Funding**	
☐ **Federal Funding**, including flow-through federal funding (i.e., NIH, NSF, DoD, etc.)	Name of funding source:
	Institutional Proposal or Award Number:
	eDoc # (for multi-site projects):
☐ **Industry Funding**	Name of funding source:
	Institutional Proposal or Award Number:
	eDoc #:
☐ **Foundation Funding**	Name of funding source:
	Institutional Proposal or Award Number:
☐ **Department Funding**	Name of funding source:
☐ **Gift Funding**	Name of funding source:
☐ **Other**	Name of funding source:

5.0 Resources Available to Conduct the Human Research:

Describe the resources (facilities, time, emergency resources, etc.) available to recruit, consent, conduct study procedures, and analyze data.

All recruitment, consent, study procedures and data analysis will be conducted by study investigators at BUMC Phoenix.

6.0 Study Population:

6.1 Select all the categories of participants included in the research:

☒ Healthy adults	☐ Non-English-speaking subjects
☒ Non-healthy adults	☐ UA staff/faculty
☐ Children (under 18 years old) *	☐ UA students
☐ Pregnant women, neonates, and/or fetuses*	☐ Banner employees
☐ Prisoners*	☐ Refugees
☐ Native Americans, Alaskan Native, and Indigenous Populations*	☒ Other – please explain: All patients admitted to BUMCP toxicology service diagnosed with RSE
☐ Adults unable to consent (i.e., cognitively impaired adults) *	

6.2 For each of the above selected categories, describe the inclusion and exclusion criteria. Indicate age range, gender, and ethnicity.

Inclusion Criteria

1. Ages ≥ 18 years.
2. Able to speak and understand English.
3. RSE requiring IV pain medication for NRS pain score > 5.
4. No allergy to ketamine or fentanyl.
5. Ability to provide informed consent.
6. ≤ 24 hours from envenomation.

Exclusion Criteria

1. Pregnant or lactating.
2. Prisoners.
3. Refugees.
4. History of schizophrenia.
5. Clinically intoxicated.
6. On buprenorphine therapy.
7. History of uncontrolled hypertension.
8. Increased intracranial pressure.
9. Systemic envenomation.

6.3 Describe the total number of subjects to be enrolled locally. If obtaining specimens, specify the maximum number of specimens needed for this project.

40 participants.

6.4 Select the methods used to recruit individuals.

☐ Email	☒ Screening of the Electronic Medical Record (EMR)

☒ Face to face	☐ Social media
☐ Flyers	☐ SONA System
☐ In person presentations	☐ TV, Radio, Print
☐ Online advertisements	☐ Other – please explain: Click or tap here to enter text.
☐ Phone calls	

6.5 Explain the recruitment process. Describe how potential subjects will be identified, where recruitment will take place, when recruitment will occur, and the methods that will be used to recruit individuals.

Subjects will be identified by the study investigators who are BUMCP physician medical toxicologists and care for RSEs at BUMCP. Subjects will be screened and interviewed using the inclusion/exclusion criteria and if eligible, be asked if they would like to participate in the study. The informed consent form will be reviewed by a trained investigator with the subject/legally authorized representative. To include the voluntary nature of the study, risks/benefits, and study procedures will be explained in detail. Adequate time to review the informed consent form will be given and all questions and concerns will be addressed. The subject/legally authorized representative be given a copy of a signed consent if they choose to participate.

7.0 Consenting Process:

7.1 Indicate the informed consent process(es) and/or document(s) for the study. Check all that apply.

Written Consent
☐ Informed Consent (ICF) – written or electronically signed form
☐ Parental Permission – written or electronically signed form
☐ Assent (participants under 18) – written or electronically signed form
☒ Combined ICF/PHI Authorization – written or electronically signed form
☐ Protected Health Information (PHI) Authorization – written or electronically signed
☐ Translated Consent/Assent – written or electronically signed form(s)
☐ Short Consent Form – written or electronically signed form (see guidance on **Short Form process**)
☐ Debriefing Script or Form – document used to properly inform subjects of the study's purpose when intentionally deceived

Oral/Online/Unsigned Consent (Appendix for Alteration/Waiver of Consent or PHI is Required)
☐ Informed Consent – oral script/online/unsigned
☐ Parental Permission – oral script/online/unsigned
☐ Assent – oral script/online/unsigned
☐ Translated Consent/Assent – oral script/online/unsigned

Waivers of Informed Consent and/or PHI Authorization
☐ Waiver of Consent
☐ Full Waiver of PHI Authorization
☒ Partial Waiver of PHI for Screening Purposes

7.2 Describe in detail the consent processes checked above, including any waiting period for subjects to sign the consent, steps to minimize the possibility of coercion or undue influence, and the language used by those obtaining consent.

The informed consent form will be reviewed by a trained investigator with the subject/legally authorized representative. To include the voluntary nature of the study, risks/benefits, and study procedures will be explained in detail. Adequate time to review the informed consent will be given, all questions and concerns will be addressed. If the subject/legally authorized representative choose to participate they will be asked to sign the paper informed consent form and will be given a copy of the signed consent form.

7.3 Where will the original signed consent and PHI authorization documents be stored?

Locked file cabinet in the office of the PI.

7.4 Acknowledgement of consent form storage.

☒ I will store original signed consent and/or PHI authorization documents for at least 6 years past the time the study is concluded.
☐ For studies involving minors, I will store original signed consent and/or PHI authorization documents for at least 6 years after the youngest participant turns 18.
☐ Not applicable – I am not collecting signed documents.

8.0 Research and Data Collection Procedures:

8.1 Select the methods of data collection that will be used in this study (select all that apply):

☐ Anthropometric measures (e.g., height, weight, waist circumference, etc.)	☐ Participant observation

☐ Audio/video recording	☐ Screening data
☐ Benign interventions	☐ Self-health monitoring (e.g., pedometers, food diaries, etc.)
☐ Biological specimens – blood draws	☐ Surveys – paper
☐ Biological specimens – clinically discarded blood or specimens	☐ Surveys – internet (including online and email-based data collection)
☐ Biological specimens (urine/feces, tissue, saliva, skin, hair, nails, nasal swab)	☐ Surveys – telephone
☐ Clinical Data Warehouse (CDW)	☒ Randomization with control and experimental groups
☐ Cognitive or behavioral measures, including daily diaries	☐ Records – billing
☐ Data collected using other communication/electronic devices (e.g., cell phones, pagers, and texting devices)	☐ Records – educational
☐ Data previously collected for research purposes	☐ Records – employee
☐ Deception	☐ Records – lab, pathology and/or radiology results
☐ Instrumentation, equipment, or software not approved by the FDA	☐ Records – mental health
☐ Interviews – focus groups	☐ Records – substance abuse
☐ Interviews – in person	☐ Research imaging protocols
☐ Interviews – virtual/online	☐ Recombinant DNA
☒ Medical records review	☐ Social networking sites
☐ MRI/ultrasound with contrast	☐ Stem cells
☐ MRI/ultrasound without contrast	☐ Radiation Scans (X-Ray, CT Scans, etc.)
☐ Non-invasive instruments (e.g., external sensors applied to the body)	☒ Other activities or interventions – describe: Investigators will obtain pain response scores (pain NRS, RASS, SERSDA), and monitor the subject at bedside

8.2 Description of research procedures.

Data to be abstracted from medical records include:

Demographic information

Age

Gender

History

Weight

PMH

Allergies

Home medications

Substance use

If yes what? alcohol, opioid, stimulant, hallucinogen, marijuana, tobacco

Clinical/treatment

HPI including time of bite, type of snake (if known), field treatments, ED treatment, vital signs, labs, imaging, medications administered and time (including analgesia), antivenom administration (time from bite to AV, type of AV, doses, and vials), procedures (i.e., splinting), measurements, adverse events, LOS

Study specific data

Randomization drug (either ketamine or fentanyl)

Group A - Ketamine

A single dose of ketamine 0.3 mg/kg IV over 15 minutes.

Group B - Fentanyl

A single dose of fentanyl 1mcg/kg IV, maximum 100 mcg, over 15 minutes.

Time drug given

Data obtained prior to med administration and then following medication administration at intervals of 15, 30, 60 and 120 minutes

- Record vital signs (HR, B/P, resp rate, O2 sat)
- Obtain and assess pain response scores
  1. Pain Numerical Rating Score (NRS – 0-10)
  2. Richmond Agitation Sedation Scale (RASS)
  3. Side Effect Rating Scale for Dissociative Anesthesia (SERSDA)

The SERSDA score has been used in multiple studies to evaluate the side effects of ketamine [4].

- Record any airway interventions required?

  If yes what? new supplemental O2/BVM/intubation, jaw thrust

- Record any rescue meds, dose and time

Rescue medication - Fentanyl

1 mcg/kg IV fentanyl (0.5 mcg/kg if age >55 yrs)

Defined as rescue if given <30 min post study intervention for pain score >5 or patient requesting additional medication.

Patient pain satisfaction score at discharge

Instrument Administration

Patients meeting inclusion criteria will be identified by the study investigators who are BUMCP physician medical toxicologists and care for RSEs. Informed consent, randomization and data abstraction/collection will be obtained by the investigators. Pain scores will be obtained at bedside by investigators at the following intervals; prior to medication administration (zero) and after medication administration at the following intervals 15, 30, 60, and 120 minutes, and a patient satisfaction score at discharge.

Randomization

Block randomization – A randomization list has been developed that will be used to assign drug (form: 'Master List-Randomization'). Following enrollment, the subject will be assigned in sequential order. Each block will alternate between each drug (ketamine or fentanyl). Subjects will have 50/50 chance of being assigned to ketamine or fentanyl and will be blinded to which drug they received during the study. After participation in study (meaning they have completed their patient satisfaction score at discharge) subjects will be told what medication they received during the study.

Statistical Methods

Differences between pain scores at time zero (before drug administration) and at time 30 minutes will be compared between the fentanyl and ketamine group using a Wilcoxon Signed Ranks Test, using a two-tailed alpha of 0.05.

Significant clinical difference will be defined as an absolute difference between groups of greater than 1.3 (using confidence interval of 95%). This difference is commonly accepted as the minimum clinical difference in subjective pain scales [5].

Group Size Calculations

This is a pilot study to demonstrate feasibility, and the number of subjects (N) is determined by availability of subjects over a one-year period. Therefore, we will enroll 40 subjects. Results of this study can be used to plan a larger study with more statistical power.

Data Monitoring

Ongoing data monitoring will be performed by investigators throughout the duration of the study period.

8.3 Specify the total estimated time commitment for subject participation, and the estimated time commitment for each activity.

Total time commitment	95 minutes
Study procedures	Time to complete
Informed consent	30 minutes
Randomization	5 min
Assessment of pain scores at bedside	
Prior to drug administration (zero)	10 min
15 min after drug	10 min
30 min after drug	10 min
60 min after drug	10 min
120 min after drug	10 min
Patient pain satisfaction question at discharge	10 min

8.4 If any biological specimens (blood, urine, tissue, etc.) are being collected for research, state the amount, method, frequency, and type of specimen to be collected and what the specimen will be used for.

NA

9.0 Potential Benefits to Subjects:

9.1 Describe the anticipated benefits of this study to society, academic knowledge, or both.

This study will help increase medical knowledge about pain responses from two different medications (ketamine and fentanyl) in the treatment of pain after rattlesnake envenomation (RSE).

9.2 Describe any benefits that individuals may reasonably expect from participation (not including compensation, which cannot be considered a benefit of participation).

Subjects are not expected to receive any benefits for participation.

10.0 Risks to Subjects:

10.1 Describe all physical, psychological, social, legal, and/or economic risk that could be associated with participation in this research.

There is a potential risk of breach of confidentiality due to access and use of PHI for study data collection. All efforts are in place to ensure privacy of subject data is secure.

Participation in the study will not increase risk of adverse events compared to standard of care in the treatment of RSEs. Risks of standard treatment include adverse reactions from antivenom, which include allergic reactions, anaphylaxis, and serum sickness. Standard treatment also includes opioid analgesia such as fentanyl.

Risks include the potential side effects of the pain medication being given including but not limited to sedation, dysphoria (discomfort, distress, or unease), nausea, vomiting, muscle rigidity, respiratory depression, apnea, dizziness, blurred vision, diaphoresis, pruritis, urticaria, bradycardia, tachycardia, hypertension (high blood pressure), hypotension (low blood pressure), and laryngospasm (sudden spasm of the vocal cords).

Group A - Ketamine

A single dose of ketamine 0.3 mg/kg IV over 15 minutes.

Ketamine has been shown to be non-inferior in the treatment of multiple other painful conditions in similar hospital and emergency department settings. Ketamine has known side effects, including dysphoria, hypertension, and tachycardia, which are reduced when administered over 15 minutes compared to an intravenous push dose. Therefore, a 15-minute infusion will be used in the study. Ketamine is already commonly used for pain management within the hospital and carries a lowered risk of addiction compared to opiates such as fentanyl.

Group B - Fentanyl

A single dose of fentanyl 1mcg/kg IV, maximum 100 mcg, over 15 minutes.

Fentanyl is a common opioid analgesic medication used for acute painful conditions. Fentanyl may cause respiratory depression, apnea, blurred vision, diaphoresis, dizziness, pruritis, urticaria, muscle rigidity, nausea, vomiting, and hypotension in high doses.

Rescue medication - Fentanyl

1 mcg/kg IV fentanyl (0.5 mcg/kg if age >55 yrs)

Defined as rescue if given <30 min post study intervention for pain score >5 or patient requesting additional medication.

10.2 Discuss what steps will be taken to minimize risks to subjects/data.

Subjects will be monitored closely by study investigators during the study.

11.0 Costs, Compensation, and Injury:

11.1 Describe any costs, monetary and non-monetary, that subjects may incur. This includes time.

There is a cost of time for subjects to participate in the study.

Discuss the amount of compensation (monetary and/or non-monetary) subjects may receive. Describe if compensation will be prorated.

Subjects will not be compensated for participation.

12.0 Privacy of Subjects and Confidentiality of Data:

12.1 Describe steps, if any, to protect the privacy of the subjects throughout their participation (e.g., during the recruitment process, consent process, and/or research procedures).

All study related discussion will be conducted in private rooms. In order to maintain subject privacy, study records will be coded with unique study ID/number. Confidentiality of subjects will be maintained through the study.

12.2 Describe if data or specimens will be kept for future research, including unspecified future research and genetics. If data or specimens will be stored in a repository, indicate who holds the repository and what information will be sent to the repository. Ensure this information is reflected in the subject's informed consent form.

Data will be stored for the purpose of the pilot study.

12.3 Discuss how study results will be shared with subjects, families, and/or the institution, both immediately and long-term.

Data will not be shared with subjects/legally authorized representatives, families and/or the institution since this pilot study mainly serves to gather data for designing future studies.

12.4 Indicate if the research team will be accessing any of the following records.

☐ Substance abuse records (HIPAA and 42 CFR Part 2)
☒ Medical records (HIPAA)
☐ Educational records (FERPA)*

☐ Employee records (ABOR Policy 6-912)*
☐ Other, specify: Click or tap here to enter text.

***Access to information from a University of Arizona employee record or FERPA information requires the written permission of the participants.**

12.5 For each record source selected above, summarize the data elements to be accessed, who will access them, and how the information will be obtained.

Study data will be accessed from Banner CERNER by study investigators only.

Data will be abstracted and recorded on a pre-designed data collection form. Data will subsequently be entered on a spreadsheet by an investigator.

Patients meeting inclusion criteria will be identified by the study investigators who care for RSEs at BUMCP. Informed consent, randomization and data abstraction/collection will be obtained by the investigators. Pain scores will be obtained at bedside by investigators at the following intervals; prior to medication administration (zero) and after medication administration at the following intervals 15, 30, 60, and 120 minutes, and a patient satisfaction pain survey at discharge.

Medical records will be used/accessed by investigators. Pain response scores = pain numerical rating score (NRS – 0-10), Richmond Agitation Sedation Scale (RASS), and Side Effect Rating Scale for Dissociative Anesthesia (SERSDA). The SERSDA score has been used in multiple studies to evaluate the side effects of ketamine [4].

12.6 Indicate where data will be stored:

☐ Box@UA	☐ OnCore
☐ Box@UA Health	☐ PACS medical imaging software
☐ Clinical Data Warehouse (CDW)	☒ Password Protected Drive
☐ Cloud Server	☐ REDCap
☐ Department Drive	☐ Transmitting/receiving subject data to/from an outside group
☒ Department Office	☐ UA Records Management & Archives
☐ Encrypted Drive	☒ Banner Server/Platform, specify: password protected Word document and Excel spreadsheet secured on Banner computer
☐ External Drive (hard drive, USB, disk)	☐ Other, specify: Click or tap here to enter text.
☐ Google Suite for Education	

12.7 For EACH of the storage locations checked above, discuss the type of data to be stored, including if the data is identifiable, coded, or de-identified upon storage. Discuss who may have access to the data and how long the data will be kept.

Human subjects' names and medical record numbers will be assigned/maintained by member of the study team on a password protected Word document secured on Banner computer, accessible only by members of the study team and will be linked to all data collected with a unique study identification number. All data will then be subsequently entered into a password protected Excel spreadsheet by a study team member and will be maintained for at least 6 years. No data will be stored in UA platforms.

Consents and data collection forms will be stored separately in a locked file cabinet in the office of the PI accessible only to the study team.

12.8 Describe what security controls (e.g., administrative, physical, technical) are in place to make sure data/specimens are secure.

Banner computers are password protected and accessed only by authorized staff. All study documents saved on Banner computers will be password protected and accessed only by study team.

12.9 Indicate how data/specimens will be shared with collaborating entities:

☒ Data and/or specimens will not be shared between UA and any outside group or collaborating entity.
☐ Data/or specimens will be transmitted and/or disclosed to an outside group or a collaborating entity.
☐ Data and/or specimens will be received from an outside group or a collaborating entity.
☐ PHI will be transmitted to or received from an outside group or a collaborating entity. *
☐ A Limited Data Set will be transmitted or received from an outside group or a collaborating entity. *
☐ Data/specimens will be sold to pharmaceutical companies.

12.10 Describe what information will be shared, who it will be shared with, and how it will be shared (e.g., secure file transfer, REDCap, etc.):

NA

13.0 Additional Questions (complete as applicable):

13.1 Subject Injury: If the research involves more than minimal risk to subjects, describe the provisions for medical care and available compensation in the event of research related injury. If the Human Research has a clinical trial agreement, this language should reflect what is stated in the agreement.

The investigators have no funds set aside for the payment of treatment expenses for this study. The study is examining pain outcomes from the commercially available drugs. If injury is experienced by subjects, they may be treated by the investigator as part of standard care.

13.2 Withdrawal of Subjects: Discuss how, when, and why subjects may be removed from the study. If abrupt withdrawal is necessary, discuss how subjects will be withdrawn so that they are not put at increased risk. Discuss what happens if a subject is withdrawn from one part of the study but asked to continue with other parts, such as ongoing follow-up.

Subjects may be withdrawn from study by investigators at any time if patient is at increased risk. Subjects can also withdraw consent at any time. Subjects will then continue to be monitored as part of standard care and data collected for the study may be used for the analysis.

13.3 Monitoring for Subject Safety: Provide a brief lay discussion of your plan to monitor for subject safety. Describe what safety information will be collected, including serious adverse events, how safety information will be collected, and the frequency of collection including a timeline of when the data and review(s) will occur, who will review the information, and the plan for reporting findings.

If there will not be a way to monitor for subject safety, please explain.

Subjects will be monitored for safety at the study visit by investigators. Follow up monitoring will be done as part of routine care.

Adverse events will be monitored to ensure the safety of each subject while on the study. The site investigator will report any unanticipated adverse events to IRB according to their reporting requirements.

13.4 Data Management Plan: Please discuss the data management plan if required by your funding agency. For additional resources, reference the HSPP Data Management webpage.

NA

13.5 International Research: Describe site-specific regulations or customs affecting the research, local scientific and/or ethical review structures that differ, and if community advisory boards are involved. If so, describe their composition and involvement. For research being conducted outside of the US, please explain any local laws, regulations, or customs the IRB needs to be aware of.

NA

Additional items needed for review:

- Word Versions of applicable subject materials: Consents, PHI Authorization Form(s), Recruitment Materials, Data Collection Materials, additional Participant Materials
- Current PI/Co-PI CVs or biosketch
- Advisor approval (if the PI is a student or medical resident)
- Department/Center/Section Review approval
- Scientific/Scholarly review approval
- Responsible physician approval (if the PI is conducting medical procedures for which he/she is not clinically certified to perform)
- Additional approvals, as needed (e.g., RIA/Banner feasibility, Export Control, Radiation, COI, UA travel registry, CATS, SRC, school district approval, tribal approval, etc.)

Other items as applicable:

- HSPP Appendices
- Data Monitoring Charter and Plan
- Drug/Device information
    - Applicable drug or device appendix
    - Investigator's Brochure, drug product sheet, device manual, user's manual, instructions for use, package insert, IND/IDE documentation, FDA 1572 form, 510k indication, FDA exemption, sponsor determination of device risk, etc.
- Multi-site information (for sites engaged in research where the UA is the IRB of record)
    - Appendix for Multi-site Research
    - Documentation of reliance
    - Copy of the site's human subjects training policy
    - CV and medical license (if applicable) of site PI
- Sponsor protocol, if separate from this form