Official Title:	**A Randomized Clinical Trial of Buzzy versus Vapocoolant in Pain Relief during a venipuncture procedure in a pediatric Emergency Room**
NCT number:	unavailable
Document Type:	Study Protocol (HRP 503) and statistical plan
Date of the Document:	December 2, 2020

Complete Research Protocol (HRP-503)

Table of Contents

Template Instructions

Sections that do not apply:

- *In several sections, the addition of checkboxes for **Not Applicable** have been added to the template as responses.*
    - *If an N/A checkbox is present, select the appropriate justification from the list.*
    - *If an N/A checkbox is not present, or if none of the existing checkboxes apply to your study, you must write in your own justification.*
- *In addition:*
    - *For research where the only study procedures are records/chart review: Sections 19, 20, 22, 23, 24, 25, 31, and 32 do not apply.*
    - *For exempt research: Sections 31 and 32 do not apply.*

Studies with multiple participant groups:

- *If this study involves multiple participant groups (e.g. parents and children), provide information in applicable sections for each participant group. Clearly label responses when they differ. For example:*

  Response:

  Intervention Group:
  Control Group:

Formatting:

- *Do not remove template instructions or section headings when they do not apply to your study.*

If you are pasting information from other documents using the "Merge Formatting" Paste option will maintain the formatting of the response boxes.

Amendments:

- *When making modifications or revisions to this and other documents, use the **Track Changes** function in Microsoft Word.*
- *Update the version date or number **on Page 3.***

PROTOCOL TITLE:

Include the full protocol title.

Response:

A Randomized Clinical Trial of Buzzy versus Vapocoolant in Pain Relief during a venipuncture procedure in a pediatric Emergency Room

PRINCIPAL INVESTIGATOR:

Name
Department
Telephone Number
Email Address

Response:

Name: Jill C Fennell MD

Department Division of Emergency Medicine

John R. Oishei Children's Hospital

Telephone No: 716-323-0055

Email Address jillfenn@buffalo.edu

VERSION:

Include the version date or number.

Response: Version 3.0

Version date: December 2, 2020

GRANT APPLICABILITY:

Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.

NOTE: This question does not apply to studies funded by a sponsor contract.

Include a copy of the grant proposal with your submission.

Response:

This study is not funded

RESEARCH REPOSITORY:

Indicate where the research files will be kept, including when the study has been closed. The repository should include, at minimum, copies of IRB correspondence (approval, determination letters) as well as signed consent documents. This documentation should be maintained for 3 years after the study has been closed.

Response:

Location: Conventus building, Research office, Room 5201

Address: 1001 Main Street, Buffalo NY

Department: UBMD Pediatrics, Division of Emergency Medicine

1.0 Objectives

1.1 Describe the purpose, specific aims, or objectives of this research.

Response:

The purpose of this study is to compare the anxiety and pain levels of patients when using Buzzy with ice wings, Vapocoolant, and placebo during venipuncture procedure in pediatric patients.

1.2 State the hypotheses to be tested, if applicable.

NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Response:

We hypothesize that the Buzzy will provide greater pain relief based on patient self-report and parent report of their child's pain as well as independent observation when compared to Vapocoolant or placebo.

2.0 Scientific Endpoints

2.1 Describe the scientific endpoint(s), the main result or occurrence under study.

NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should ***not*** *be a date.*

Response:

Our primary outcome is that Buzzy will have a greater degree of reduction of anxiety and pain levels compared to vapocoolant or placebo.

3.0 Background

3.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.

Response:

Among pediatric patients, phlebotomy and intravenous cannulation are two important sources of self-reported pain in the pediatric ED. Unmanaged needle stick pain has been associated with needle phobia, greater pain with future sticks; anxiety associated with other medical procedures, healthcare avoidance and increased adult pain sensitivity (Lunoe, 2014; Cohen 1997; Hamilton, 1995; Pate, 1996). Various methods have been proposed for management of acute pain associated with these medical procedures. Pharmacological methods include EMLA, lidocaine and ethyl chloride (vapocoolant). Behavioral methods such as information provision, distraction, sensory focusing, and cognitive behavioral therapy (CBT) have also been utilized (Blount, 2009). Optimization of pain control during phlebotomy and IV catheterization in the Pediatric ED is essential in an effort to avoid the aforementioned adverse effects of needle insertion. In the pediatric ED, quick acting methods are favored over those requiring time to act such as EMLA and CBT.

Vapocoolants, volatile refrigerated liquids such as ethyl chloride, are a frequent choice in many pediatric EDs, including our own, prior to phlebotomy or IV cannulation. Despite this, research has offered conflicting results as to their efficacy. Hogan and her colleagues conducted a systematic review of Vapocoolant in both children and adults and concluded that their "…results demonstrated that Vapocoolants are ineffective in children when compared to placebo or no treatment" (Hogan ,2014). Shah, Taddio & Rieder have hypothesized that the sensation of cold on their skin is perceived by children as painful (Shah, 2009).

Recently several labs have introduced hand held devices based on Melzack and Wall's Gait Control theory (Melzack 1965) which asserts that activation of non-nociceptive fibers can interfere with signals from pain fibers thereby inhibiting pain. This theory helps to explain why rubbing or massaging a painful area of skin can lessen the pain. One such device is the Buzzy.. The Buzzy is a vibrating palm-sized device with removable ice wings developed by MMJ Labs Atlanta, GA.

The Procedure Behavior Checklist (PBCL) is a well-established observational pain measure that has been validated for children 3-18 years old. It evaluates both the intensity and frequency of 10 defined behaviors that indicate distress. The PBCL was developed by Katz et al in 1980. On a scale of 1-5, it rates child's muscle tension, screaming, crying, restraint needed, verbalized pain, anxiety, etc. The scores are then added together to give a final score. The Faces Pain Scale – Revised (FPS- R; Hicks et al 1990) is a self-report measure used to assess the intensity of children's pain. It consists of 6 faces, with each one representing an increasing degree of pain moving from left to right in increments of two starting from zero (0, 2, 4, 6, ,8, 10).

Both of the PBCL and Faces pain scale –revised have been validated tool and used frequently in clinical practices and studies when evaluate patient's pain scale.

In this study, we will compare the effectiveness of pain release devices i.e. buzzy, with vapocoolants or placebo. We will use the validated PBCL and Faces pain scale-revised methods as the pain evaluation tools. To our knowledge, no study has been performed on comparison of the effectiveness of these commonly used pain release devices. We hope to contribute some useful information in this field through our research.

3.2 Include complete citations or references.

Response:

Bijttebier P, Vertommen H. (1998). The impact of previous experience on children's reactions tovenipunctures. Journal of Health Psychology, 3 (1):39– 46.

Blount R. L., Zempsky W. T., Jaaniste T., Evans S., Cohen L. L., Devine K. A., Zeltzer L. K. Management of pain and distress due to medical procedures. In: Roberts M C, Steele R, editors. Handbook of pediatric psychology. 4th Ed. New York: Guilford Press; 2009. pp.171–188.

Cohen Reis E. &and Holubkov R. (1997). Vapocoolant spray is equally effective as EMLA cream in reducing immunization pain in school-aged children. Pediatrics, 100 (6).

Hamilton J.G. (1995). Needle phobia: A neglected diagnosis. Journal of Family Practice, 41 (2):169-175.

Hicks C.L., von Baeyer, C.L., Spafford P.A., van Korlaar I. & Goodenough B. The Faces Pain Scale - Revised: toward a common metric in pediatric pain measurement. Pain 93(2001) 173-183.

Lunoe M.M, Drendel A.L., Levas M.N., Weisman S.J., Dasgupta M., Hoffman, R.G. & Brousseau D.C. (2015). A randomized clinical trial of jet-induced lidocaine to reduce venipuncture pain for young children. Annals of Emergency Medicine, 66 (5), 466-474.

Melzack R. & Wall P.D. (1965). Pain mechanisms: A new theory. Science, 150: 971-979.

Pate J.T., Blount R.L., Cohen L.L. & Smith A.J. (1996). Childhood medical experience and temperament as predictors of adult functioning in medical situations. Child Health Care, 25 (4): 281-298.

Shah V., Taddio A. & Rieder M.J. (2009). Effectiveness and tolerability of pharmacologic and combined interventions for reducing injection pain during routine childhood immunizations: Systematic review and meta-analyses. Clinical Therapeutics, 31 (Supplement 2), S104-51.

Katz, E.R., Kellerman, J., & Siegel, S.E. (1980). Behavioral distress in children with cancer undergoing medical procedures: Developmental considerations. Journal of Consulting and Clinical Psychology, 48, 356-365.

LeBaron, S. & Zeltzer, L. (1984). Assessment of acute pain and anxiety in children and adolescents by self-reports, observer reports, and a behavior checklist. Journal of Consulting and Clinical Psychology, Vol 52, No. 5, 729-738.

QFAB Bioinformatics. (2015). ANZMTG Statistical Decision Tree, Power Calculator. (Version 1.0) [Web Application]. Retrieved from http://www.anzmtg.org/stats/PowerCalculator

4.0 Study Design

4.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).

Response:

This is a single-center, randomized, open label, placebo controlled clinical trial.

5.0 Local Number of Subjects

5.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.

Response:

We will enroll 168 patients in the study with 56 in each arm.

5.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).

Response:

We anticipate screening about 500 patients to reach our target sample.

5.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Response:

The Emergency Department at John R Oishei Children's Hospital has an annual volume of 45,000 to 50, 000 patients, with at least 1/10 of them receiving venipunctures procedure including IV's line placement or phlebotomy procedure for various reasons. We anticipate that we can easily enroll 168 subjects within 24 months.

6.0 Inclusion and Exclusion Criteria

*6.1 Describe the criteria that define who will be **included** in your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

Inclusion criteria:

1. Male or female patients 6 to18 years old

2. Need venipuncture procedure including IV's line placement and/or phlebotomy at the ED.

*6.2 Describe the criteria that define who will be **excluded** from your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

Exclusion criteria include:

1. Patients is sensitive to cold i.e. Raynaud's disease.

2. Sickle cell disease, diabetic

3. Critically ill patients

4. Mentally challenged patients

5.. GCS< 15

6.. Patient with altered sensation

7.. Patients needing more than one attempt for IV placement or phlebotomy

6.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.

NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.

Response:

☐ Adults unable to consent

☒ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

6.4 Indicate whether you will include non-English speaking individuals in your study. ***Provide justification if you will exclude non-English speaking individuals.***

*In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may **not** be routinely excluded from research as a matter of convenience.*

In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.

Response:

This study will not include patients whose legal guardians do not speak English. Children with parents/legal guardians who cannot speak and read English will be encountered infrequently. They represent diverse language groups and translating consent documents as well as translating pain scale surveys into many languages would be impractical for this unfunded study. Meanwhile, it is impractical for us to have two people who speak the same non-English language during the recruitment phase with one being the person who obtains the consent and one being the witness per our IRB request at any given time.

By not including non-English speaking subjects in this study, we are not withholding any benefit from these patients. Meanwhile, we do not anticipate that we add any burden to the patients who are enrolled in the study.

The main purpose of this study is to compare the effectiveness of pain relief using different methods, the Buzzy, vapocoolant and placebo. Patient enrolled in the study will randomly assigned into one of the three different study groups, Buzzy Bee with ice wings, vapocoolant or placebo. For eligible patients that are not enrolled in the study, they may also receive buzzy, or vapocoolant intervention, depending on the bedside nurse's discretion, as these methods have been frequently used by our ED nurses to help patients for pain relief. So regardless weather a patient is enrolled in the study or not, he/she may receive the similar pain relief method for IV line placement or phlebotomy procedure.

Thus, we will exclude subjects whose legal guardians do not speak English from the study due to the above mentioned reasons. We believe that we will not withhold any benefit from non-participants, nor add any burden to the participants by not enrolling non-English speaking patients in the study.

7.0 Vulnerable Populations

If the research involves special populations that are considered vulnerable, ***describe the safeguards included to protect their rights and welfare.***

NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.

7.1 For research that involves ***pregnant women,*** *safeguards include:*
NOTE CHECKLIST: Pregnant Women (HRP-412)

Response:

☒ **N/A**: This research does not involve pregnant women.

7.2 For research that involves ***neonates of uncertain viability or non-viable neonates,*** *safeguards include:*
NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)

Response:

☒ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

*7.3 For research that involves **prisoners**, safeguards include:*
NOTE CHECKLIST: Prisoners (HRP-415)

Response:

☒ **N/A:** This research does not involve prisoners.

*7.4 For research that involves **persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")**, safeguards include:*
NOTE CHECKLIST: Children (HRP-416)

Response:

We will obtain consent from legal guardian for subject who is younger than 18 years of age.

☐ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

*7.5 For research that involves **cognitively impaired adults**, safeguards include:*
NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)

Response:

☒ **N/A:** This research does not involve cognitively impaired adults.

*7.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable. **Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response:

No other specifically targeted populations will be enrolled in this project.

8.0 Eligibility Screening

*8.1 Describe **screening procedures** for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

📎 *Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).*

Response:

We will use a screening sheet to help our physician identify patient's eligibility. The screening sheet is the first page of the data collection form.

☐ **N/A:** There is no screening as part of this protocol.

9.0 Recruitment Methods

☐ **N/A:** This is a records review only, and subjects will not be recruited.
NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

9.1 Describe when, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).

Response:

Our study team will screen potential eligible patient by monitoring the patients' Tracking Shell (OCH All Beds Only view) in the password protected Power chart system at the ED of John R. Oishei Children's Hospital. Patient needs blood work or IV fluid /medication treatment will be screened for eligibility.

9.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself.

Response:

Our research team will approach the patient and the legal guardian in a patient's private room at the ED. The consent process will be done when no other staff is in the room.

9.3 Identify any materials that will be used to recruit subjects.

NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.

For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.

Response:

No materials will be used for recruitment for this study.

10.0 Procedures Involved

*10.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.

Response:

Randomization of subject into one of the three study arms

There will be three arms of this study with each arm testing a different pain reducer: Buzzy Bee, Vapocoolant, and placebo. We will use a sham device e.g. a band around the arm for placebo control.

After obtaining informed consent, the patients will be randomized into one of the three groups following a randomization table created by a statistician. Whichever intervention is randomly selected will be performed on patient prior to the needle stick.

These methods have been used in the ED as part of routine procedures to help patient for pain relief from a needle stick, the RNs are familiar with these methods. However, for the purpose of this study, the training videos will be uploaded in the Kaleidascope Talent management for RNs to review the procedure and help them to refresh their memories.

Videotaping of subject

Using a camera, an ED research assistant will videotape subject's whole body including the facial expression while phlebotomy and IV catheter placement is performed for scoring of the PBCL. We will tape the entire venipuncture procedure starting from sterilization and ending at the time when the venipuncture is completed. If the first venipuncture procedure attempt is failed, we will not tape the second attempt. This subject will be withdrawn from the study.

Obtaining pain scores from subject and legal guardian using the Faces Pain Scale-Revised instrument

Before and after the venipuncture procedure, we will ask the legal guardian and subject to complete a Faces pain scale revised form. Since the revised form is validated to use for both adult and children, the same document will be used for the legal guardian and children for this study. This document is attached with this submission.

Reviewing of the videotape

Two physicians will review the video tape independently, and give a score using the PBCL tool. These two physicians are blinded to the study aims. They will be trained on how to use the PBCL by the PI.

In the event when there is a discrepancy of the PBCL score between the two reviewers, the mean of the two scores will be used as the final score.

10.2 Describe what data will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.

Response:

We will collect demographic data, reason for venipuncture, PBCL score, facial pain score etc.

10.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).

Include copies of these documents with your submission.

Response:

The following documents will be used for data collection:

1. Data collection form

2. Procedure behavior check list (PBCL)

3. The Faces Pain scale-revised document.

These documents will be submitted with this IRB application.

10.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

Response:

Kaleida health Electronic power chart records will be used for data collection.

*10.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response:

No individual subject results will be shared with the subject or others.

*10.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response:

Study results will not be shared with subjects or others. The final results of this study may be presented at a conference or published in a peer reviewed journal; however, only group data will be publicized in these circumstances, no individual identifiable information will be released.

11.0 Study Timelines

11.1 Describe the anticipated duration needed to enroll all study subjects.

Response:

We anticipate completing subject recruitment within 24 months of time.

11.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Response:

The duration of the individual subject's participation in this study will be 5-10 minutes. It will be ended when the patient completes the Facial pain scale sheet. No study follow-up will be done for this project.

11.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).

Response:

The estimated duration for the investigators to complete the study will be 16 months. We will spend 24 months to recruit subject and another 3-4 months for data analysis.

12.0 Setting

12.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.

NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."

Response:

The consenting and videotaping process will be conducted in the private patient room in the ED at John R. Oishei Children's Hospital. Data collection will be completed by our research assistant at their desk in the ED, where the ED is bandage accessed. The video tape will be reviewed at the UBMD Pediatric physician's office located on the ID badge assessed 5th floor of the Conventus building (1001 Main St, Buffalo, NY 14203).

12.2 For research conducted outside of UB and its affiliates, describe:

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research, international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.

Response:

☒ **N/A:** This study is not conducted outside of UB or its affiliates.

13.0 Community-Based Participatory Research

13.1 Describe involvement of the community in the design and conduct of the research.

NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Response:

☒ **N/A:** This study does not utilize CBPR.

13.2 Describe the composition and involvement of a community advisory board.

Response:

☒ **N/A:** This study does not have a community advisory board.

14.0 Resources and Qualifications

*14.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.*

NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.

Response:

The study PI Dr. Jill Fennell is a second year fellow physician in the Emergency Department of Oishei children's Hospital, she is a certified pediatrician. She has participated in clinical researches previously as Co-PI.

Dr. Ted Andrew and Heather Territo will be the mentors for this project. Dr. Andrew is an attending physician in general pediatrics department, and Dr. Territo is an attending in ED. Both of them have involved in numerous studies as PI and mentors in the past.

The study coordinator has more than 14 years of experience in conducting clinical researches including drug trial, device trial, observational research, double blinded randomized drug trial, chart review study etc. She is familiar with good research practice regulations and rules. She will be responsible for IRB submission and coordinating all study activities for this project.

Dr. John Pastore, a pediatric hospitalist, Dr. Kunal Chadha will be the double blinded observers. They will review the tape and give a score based on the PBCL instrument.

The statistician, Dr. Brian Wrotniak, has extensive expertise in study design and data analysis. He is responsible for study design and data analysis for this study.

Describe other resources available to conduct the research.

A group of research assistants in the ED will be involved in subject recruitment for this study under the supervision of the study coordinator.

14.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.

NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.

Response:

The research assistants work 7 days a week, 13 hours per day enrolling patients. The PI will work 1-2 hours per week to address questions related with the study. The two reviewers will work for about 2 hours per week to review the video tape.

14.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.

NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.

Response:

This study involves minimum risk to the participant. We will videotape participant's whole body during the needle stick process. We do not anticipate any consequences related with the videotaping procedure.

14.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response:

The PI, mentors and the study coordinator have involved in the development of the study protocol, they are very familiar with the study design and their duties and functions.

The Research assistants will directly work under the supervision of the study coordinator. The RAs' duties will include: screening potential eligible patient, obtaining consent/assent, videotaping patient and legal guardian as well as collecting data on data collection form.

The study coordinator will provide training to all RAs before the RAs start patient's recruitment. The training is focused on the following aspects:

1. Review study protocol by presenting the materials to the RAs with a slide show. The RAs are required to understand the study aims/purpose and the detail of the study procedures.

2. Review data collection forms. The RAs are required to know the inclusion and exclusion criteria for the study and know what kinds of patients are potentially eligible and need to be screened for the study. In addition, they will also be trained on how to collect data on the data collection form.

3. Review the consent documents. The RAs are required to know (a) the contents of the consent documents, (b) how to approach and introduce the study to the legal guardian and patient (c) how to address some of the common questions that the patient may have (d) immediately contact the study coordinator or PI for a question to which they do not know the answer.

The coordinator will ask the RAs to practice the procedures of obtaining consent at the training meeting.

4. The PI will train the study coordinator on how to use the camera to videotape patient. Then the coordinator will train the RAs about this procedure. Practice will be required as part of the training process.

The training log will reflect areas of trainings and demonstrations of competence, including the method used, e.g. role play. The trainer and trainees names will be documented in the training log as one of the regulatory documents.

All our RAs are CITI trained. They have been helping on patient recruitments for a few other studies conducted in the ED and are very familiar with the patient recruitment and consenting procedures.

15.0 Other Approvals

15.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).

Response:

☒ **N/A:** This study does not require any other approvals.

16.0 Provisions to Protect the Privacy Interests of Subjects

16.1 Describe how you will protect subjects' privacy interests during the course of this research.

NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Response:

Subject will be recruited at a private patient's room in the ED where no other people are around beside the patient, their legal guardian, and the RN who performs the needle stick.

16.2 Indicate how the research team is permitted to access any sources of information about the subjects.

*NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question **does apply** to records reviews.*

Response:

The PI and her mentors are physicians at the children's hospital, they have been granted with the right to access the electronic power chart system by Kaleida Health IST to carry out their duties as physicians. The research personnel also are granted with the right to access the power chart by Kaleida Health IST for carrying out their duties as researcher staff.

In order to screen potential eligible patient for this study, we will also apply for a partial HIPAA waiver from our IRB.

17.0 Data Management and Analysis

17.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Response:

All data analyses will be performed with SAS (version 9.2; SAS Institute, Inc., Cary, NC) and R (version 3.0.3) software. Chi-square and Fisher's exact test will be used to compare adverse events (e.g., systemic reaction, anaphylaxis, SOB, dyspnea, excess bleeding or hematoma formation), venipuncture and catheterization first attempt success, and number of patients with no to mild pain during needle insertion.

The Kruskal-Wallis test will be used to compare each of the two observers' assigned scores on the PBCL across three time periods: pre, procedure and post-procedure. Pre-procedure is defined as the time period prior to needle insertion including the placement of Vapocoolant, pain control or sham device up to needle insertion. The procedure period is defined as needle insertion through withdrawal. Post-procedure is defined as the 2 minute time period after needle withdrawal. Only patient and observer pain scores will be used for first-time needle insertion. If first attempt is failed, subject will be withdrawn from the study. . Comparisons of pain scores of the five intervention groups to placebo (sham device) will be analyzed via ANOVA.

17.2 If applicable, provide a power analysis.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

Response:

For chi-square analysis, based on a medium effect size of 0.3, alpha of 0.05, degree of freedom of 8, and 80% power it is estimated we will need a total of 168 subjects (56 per group). *(QFAB Bioinformatics. 2015)*

17.3 Describe any procedures that will be used for quality control of collected data.

Response:

Our RA will double check the data form to assure accuracy and completeness of data collection, if there is any missed data point, the RA will fill in the missing information immediately.

18.0 Confidentiality

A. Confidentiality of Study Data

Describe the local procedures for maintenance of confidentiality of ***study data and any records that will be reviewed for data collection****.*

18.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and

separation of identifiers and data, as applicable. Include physical (e.g. paper) ***and*** *electronic files.*

Response:

Completed paper data form with subject identifier and signed consent/assent documents will be placed in a locked study box in the ED. The study coordinator will collect these documents on a daily basis. The documents will be stored in a locked file cabinet in a research storage room (Conventus, Room 5201, 1001 Main Street, Buffalo, NY 14203). Each subject's data form will be labeled with a unique study identify number (ID). In addition, we will use a "**subject enrollment log**" to track subject's enrollment and data entry status. This log is attached with this submission. Subject's ID, medical record number, enrollment date, and data entry date will be entered in this log. This log will be stored in a locked file cabinet in the study coordinators' office Room 5201 in the Conventus building.

The data will be entered in a Microsoft excel spread sheet (**Database**) by a trained research assistant. Database will be saved in a password protected UPA secure online drive. No subject's name, DOB, medical record number or Fin Number will be entered in the database. The study ID number will be served as the code key to link the Database and the Subject enrollment log. We need to collect subject's medical record number for the purpose of answering query.

The study coordinator will transfer the subject's video from the camera to a password protected secure UPA online folder, which will also be shared with the two physicians who will reviewed these videos. Then the coordinator will erase the video from the camera.

The two trained physician observers will review the video saved on the password protected secure online folder at their Conventus offices and give a PSCL score for each subject. Video will be erased upon completing the study.

18.2 A. How long will the data be stored?

Response:

Videotapes will be erased upon the end of the study. Paper data form and subject enrollment log will be stored for three years after IRB closes this study. Electronic data base will be stored indefinitely.

18.3 A. Who will have access to the data?

Response:

The PI, study coordinator and research assistant that perform data entry will have access to the data. The two observers will access the video image data.

18.4 A. Who is responsible for receipt or transmission of the data?

Response:

The study coordinator will be responsible for transmitting the data.

18.5 A. How will the data be transported?

Response:

Everything will be transported manually.

B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☒ **N/A:** No specimens will be collected or analyzed in this research.
(Skip to Section 19.0)

18.6 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

Response:

18.7 B. How long will the specimens be stored?

Response:

18.8 B. Who will have access to the specimens?

Response:

18.9 B. Who is responsible for receipt or transmission of the specimens?

Response:

18.10 B. How will the specimens be transported?

Response:

19.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.

19.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Response:

This is an observational study, involves minimum risk to participant. We do not anticipate any safety issue that may be related with the participation of this study.

19.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Response:

Not applicable.

19.3 Describe any safety endpoints.

Response:

Not applicable.

19.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Response:

Not applicable.

19.5 Describe the frequency of safety data collection.

Response:

Not applicable

19.6 Describe who will review the safety data.

Response:

Not applicable

19.7 Describe the frequency or periodicity of review of cumulative safety data.

Response:

Not applicable

19.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

Response:

Not applicable

19.9 Describe any conditions that trigger an immediate suspension of the research.

Response:

Not applicable

20.0 Withdrawal of Subjects

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*20.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response:

If the first venipuncture procedure is failed, subject will be withdrawn from the study.

20.2 Describe any procedures for orderly termination.

NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

Response:

If a subject is withdrawn from the study, we will not collect any data from the subject.

20.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

Response:

If a subject withdraws from the research in the ED, no study data will be collected for the study. The signed consent/assent document will be kept in the file cabinet in the research office, Conventus building, Room 5201.

21.0 Risks to Subjects

21.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

Response:

Some subjects may find the device a discomfort, however previous studies on devices show minimal risk for discomfort or hazards. In addition, breach of confidentiality is the potential risk for this study.

21.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

Response:

Nurse will follow instruction when place the device on subject to avoid any unnecessary discomfort. In addition, please refer to section 18 A for answers on protecting data confidentiality.

*21.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response:

None

21.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response:

The devices have no known risk to embryo or fetus.

21.5 If applicable, describe risks to others who are not subjects.

Response:

None

22.0 Potential Benefits to Subjects

22.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.

*NOTE: Compensation **cannot** be stated as a benefit.*

Response:

A subject may experience less pain/ anxiety if he/she is provided with the device or the vapocoolant while the venipuncture procedure is performed.

23.0 Compensation for Research-Related Injury

☒ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

*23.1 **If the research procedures carry a risk of research related injury,** describe the available compensation to subjects in the event that such injury should occur.*

Response:

23.2 Provide a copy of contract language, if any, relevant to compensation for research related injury.

*NOTE: If the contract is not yet approved at the time of this submission, submit the current version here. If the contract is later approved with **different language regarding research related injury**, you must modify your response here and submit an amendment to the IRB for review and approval.*

Response:

24.0 Economic Burden to Subjects

24.1 Describe any costs that subjects may be responsible for because of participation in the research.

NOTE: Some examples include transportation or parking.

Response:

There is no cost for subjects to participate in this study.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

25.0 Compensation for Participation

25.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.

Response:

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

☒ **N/A:** There is no compensation for participation. This section does not apply.

26.0 Consent Process

26.1 Indicate whether you will be obtaining consent.

NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study. Consent documentation is addressed in Section 27.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 27.0)*

26.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.

Response:

The consent process will take place in the patient's private room in the ED. We will find the best time to approach the patients and their legal guardians for consenting purpose to avoid the interruption of patient's care as well as to protect patient's privacy. No other people will be in the patient's room beside the patient and the legal guardian when we obtain the consent.

26.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.

NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.

Response:

Enough time will be given to the legal guardian/participant to review the inform consent and to allow them understand the study completely, so they can make a clear informed decision. All questions will be addressed before obtaining the signatures from the legal guardian/participant.

26.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Response:

This study does not involve follow-up procedure. The legal guardian and participant will be informed that they have right to withdraw from the study at any time before the consent is being signed. The PI's contact information is listed in the informed consent.

26.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*
- *Steps that will be taken to minimize the possibility of coercion or undue influence*
- *Steps that will be taken to ensure the subjects' understanding*

Response:

☒ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

Non-English Speaking Subjects

☒ **N/A:** This study will not enroll Non-English speaking subjects.
(Skip to Section 26.8)

26.6 Indicate which language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.

NOTE: The response to this Section should correspond with your response to Section 6.4 of this protocol.

Response:

26.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

NOTE: Guidance is provided on "SOP: Informed Consent Process for Research (HRP-090)."

Response:

Cognitively Impaired Adults

☒ **N/A**: This study will not enroll cognitively impaired adults.
(Skip to Section 26.9)

26.8 Describe the process to determine whether an individual is capable of consent.

Response:

Adults Unable to Consent

☒ **N/A**: This study will not enroll adults unable to consent.
(*Skip to Section 26.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 26.9 and 26.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 26.11 and 26.12).*

26.9 Describe how you will identify a Legally Authorized Representative (LAR). Indicate that you have reviewed the "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" for research in New York State.

NOTE: Examples of acceptable response includes: verifying the electronic medical record to determine if an LAR is recorded.

Response:

☐ We have reviewed and will be following "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

26.10 ***For research conducted outside of New York State****, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

This study will not be performed outside of NYS.

26.11 Describe the process for ***assent of the adults****:*

- *Indicate whether assent will be obtained from all, some, or none of the subjects. If some, indicate which adults will be required to assent and which will not.*

Response:

- *If assent will not be obtained from some or all subjects, provide an explanation of why not.*

Response:

26.12 Describe whether ***assent of the adult*** *subjects will be documented and the process to document assent.*

NOTE: The IRB allows the person obtaining assent to document assent on the consent document using the "Template Consent Document (HRP-502)" Signature Block for Assent of Adults who are Legally Unable to Consent.

Response:

Subjects who are not yet Adults (Infants, Children, and Teenagers)

☐ **N/A**: This study will not enroll subjects who are not yet adults.
(Skip to Section 27.0)

26.13 Describe the criteria that will be used to determine ***whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in***

the research *under the applicable law of the jurisdiction in which the research will be conducted* ***(e.g., individuals under the age of 18 years)****. For research conducted in NYS, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*

NOTE: Examples of acceptable responses include: verification via electronic medical record, driver's license or state-issued ID, screening questionnaire.

Response:

This study is conducted in NYS; we will use the SOP HRP-013 as the criteria to determine if a subject is not yet an adult. We will check patient's birthdays in the electronic medical chart.

26.14 ***For research conducted outside of New York State****, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response:

This study will be conducted only in NYS.

26.15 Describe whether parental permission will be obtained from:

Response:

☒ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ Parent permission will not be obtained. A waiver of parent permission is being requested.

NOTE: The requirement for parent permission is a protocol-specific determination made by the IRB based on the risk level of the research. For guidance, review the "CHECKLIST: Children (HRP-416)."

26.16 Describe whether permission will be obtained from individuals ***other than parents****, and if so, who will be allowed to provide permission. Describe your procedure for determining an individual's authority to consent to the child's general medical care.*

Response:

Parental permission will be obtained from the subject's legal guardian who could be an individual other than the parents. These individuals need to show the legal document to

our ED registration staff for their authorities to consent the children for medical care. We will approach the patient and his/her legal guardian for study consenting purpose after the patient is being registered.

*26.17 Indicate whether assent will be obtained from all, some, or none of the **children**. If assent will be obtained from some children, indicate which children will be required to assent.*

Response:

Assent will be obtained from all children who are between 7-17 years of age.

26.18 When assent of children is obtained, describe how it will be documented.

Response:

Children will sign their names on the assent document.

27.0 Waiver or Alteration of Consent Process

Consent will not be obtained, required information will not be disclosed, or the research involves deception.

☒ **N/A:** A waiver or alteration of consent is not being requested.

27.1 If the research involves a waiver or alteration of the consent process, please review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure that you have provided sufficient information for the IRB to make the determination that a waiver or alteration can be granted.

NOTE: For records review studies, the first set of criteria on the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" applies.

Response:

27.2 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response:

28.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 29.0)

28.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

NOTE: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain

written documentation of consent. This is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.

If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).

Response:

☒ We will be following "SOP: Written Documentation of Consent" (HRP-091).

29.0 Multi-Site Research (Multisite/Multicenter Only)

☒ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

*29.1 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as:*

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*
- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response:

29.2 Describe the method for communicating to engaged participating sites:

- *Problems*
- *Interim results*
- *Study closure*

Response:

29.3 Indicate the total number of subjects that will be enrolled or records that will be reviewed across all sites.

Response:

29.4 If this is a multicenter study for which UB will serve as the IRB of record, and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods.

Response:

30.0 Banking Data or Specimens for Future Use

☒ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*30.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).

Response:

30.2 List the data to be stored or associated with each specimen.

Response:

30.3 Describe the procedures to release banked data or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Response:

31.0 Drugs or Devices

☐ **N/A:** This study does not involve drugs or devices. This section does not apply.

31.1 If the research involves drugs or devices, list and describe all drugs and devices used in the research, the purpose of their use, and their regulatory approval status.

Response:

Device:

The devices that will be used for this study are: Buzzy Bee (MMJ Labs LLC). It is a FDA approved device for decreasing pain and anxiety for vaccination shots and other venipuncture procedure in pediatric patients.

The FDA approval for the Buzzy Bee is attached with this submission.

In addition, a Fujifilm XP camera will be used for videotaping purpose.

Vapocoolant

Vapocoolant (Gebauer's ethyl chloride, Gebauer company) will be used in this study. It has also been approved by FDA to use on pediatric patient for providing local anesthesia for venipuncture procedures. A FDA approval is attached with this submission.

31.2 Describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

Response:

The Buzzy Bee and vapocoolant are stored in the medication room in the Pixis which is secured and locked; it can only be opened to those who have badge access. The Camera will be held in the same place. The Buzzy ice wing will be stored in a freezer inside of the ED.

If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

31.3 Identify the holder of the IND/IDE/Abbreviated IDE.

Response:

Not applicable.

31.4 Explain procedures followed to comply with FDA sponsor requirements for the following:

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

Response:

32.0 Humanitarian Use Devices

☒ **N/A:** This study does not involve humanitarian use devices. This does not apply.

32.1 For Humanitarian Use Device (HUD) uses provide a description of the device, a summary of how you propose to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

Response:

32.2 For HUD uses provide a description of how the patient will be informed of the potential risks and benefits of the HUD and any procedures associated with its use.

Response:

Data Management and Analysis

All data analyses will be performed with SAS (version 9.2; SAS Institute, Inc., Cary, NC) and R (version 3.0.3) software. Chi-square and Fisher's exact test will be used to compare adverse events (e.g., systemic reaction, anaphylaxis, SOB, dyspnea, excess bleeding or hematoma formation), venipuncture and catheterization first attempt success, and number of patients with no to mild pain during needle insertion.

The Kruskal-Wallis test will be used to compare each of the two observers' assigned scores on the PBCL across three time periods: pre, procedure and post-procedure. Pre-procedure is defined as the time period prior to needle insertion including the placement of Vapocoolant, pain control or sham device up to needle insertion. The procedure period is defined as needle insertion through withdrawal. Post-procedure is defined as the 2 minute time period after needle withdrawal. Only patient and observer pain scores will be used for first-time needle insertion. If first attempt is failed, subject will be withdrawn from the study. . Comparisons of pain scores of the five intervention groups to placebo (sham device) will be analyzed via ANOVA.

For chi-square analysis, based on a medium effect size of 0.3, alpha of 0.05, degree of freedom of 8, and 80% power it is estimated we will need a total of 168 subjects (56 per group). (QFAB Bioinformatics. 2015)