LETTER OF SUBMITTAL

TO: Institutional Review Board **Project #:**

FROM: David Ullman, M.D.

Project Short Title: Intranasal Midazolam in Children as a Pre-Operative Sedative – Part 2

Application for approval for research involving human subjects is attached. If approved, I agree to:

(a) obtain informed consent of all participants, unless the requirement for consent has been waived,
(b) keep a copy of the signed informed consent for each participant in the investigator's files,
(c) abide by the policy and procedure of The Mary Imogene Bassett Hospital with regard to use of human subjects in investigation,
(d) keep appropriate records concerning the subjects,
(e) operate only within the attached protocol unless prior permission is obtained in writing from the IRB,
(f) report promptly to the IRB office any unanticipated problems (adverse events) involving risk to the subject or to others, and
(g) report any unexpected deaths of subjects involved in medical treatment/intervention to the IRB office promptly. (Reporting is not required for educational or epidemiological/observational studies or surveys.)

Signed: _____
Principal Investigator date

To the best of my knowledge the information in the attached application is correct, the Principal Investigator has appropriate clinical experience/credentials to perform the work and adequate facilities/resources are available for this study.

Signed: _____
Chief of Service or Department Head date

FORM A

Application for Institutional Review Board Approval of Research Involving Human Subjects

Instructions: When selecting check boxes, please double-click on the box and select "checked" or "not checked."

General Information - Form A

Date of application: December 5, 2014 Anticipated project start date: January 2015

Principal Investigator (*PI*) (*must be permanent MIBH Staff; those appointed in training positions do not qualify*)

PI Name, Degree (*one PI only*): David Ullman, M.D.

Dept./Div: Anesthesiology

PI Fax #: 6539 PI E-mail: david.ullman@bassett.org

Office phone: 3153 Pager #: 1998 Alternate phone (*optional*):

Study Coordinator: Name: Jennifer Victory, RN E-mail: Jennifer.victory@bassett.org

Phone: 6965

Title of Project (*should be descriptive of the study*): Intranasal Midazolam in Children as a Pre-Operative Sedative

Lay summary (*In one paragraph describe the nature of the study*):
Midazolamis often given before surgery to sedate a patient before anesthesia is given. Children are often given a small dose either by mouth or squirted into the nose. Children will often spit out the oral midazolam, making it difficult to know how much medicine, if any, they have received. Giving midazolam into the nose is more reliable, but children may complain of pain, stinging, and may become upset due to the discomfort. Nosebleeds may also occur when midazolam is squirted alone into the nose. The purpose of this study is to see if adding a numbing medicine, xylocaine, to the nasal midazolam makes giving the midazolam easier and more comfortable without affecting how the midazolam works as a sedative. This is follow up to the pilot study, Project # 994. This will expand the previous study, with additional participants and revised xylocaine concentration.

☐ Externally sponsored or funded study.

Name of sponsor/funding agency:
Sponsor Contact Information:

Category of review requested:

☒ Full review
☐ Expedited – must be eligible in one of the following categories (*check categories in Appendix 3 of the Protection of Human Subjects Handbook for full descriptions)*
- ☐ 1. Clinical studies on drugs and medical devices only when condition (a) or (b) is met: (a) Research on drugs for which an investigational new drug application is not required. (b) Research on medical devices for which (i) an investigational device exemption application is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- ☐ 2. Collection of blood samples by fingerstick, heel stick, ear stick, or venipuncture.
- ☐ 3. Prospective collection of biological specimens for research purposes by noninvasive means.
- ☐ 4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
- ☐ 5. Research involving materials (data, documents, records, or specimens) that have been collected solely for nonresearch purposes.
- ☐ 6. Collection of data from voice, video, digital, or image recordings made for research purposes.
- ☐ 7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

☐ Exempt (*see Appendix 1 in the Protections of Human Subjects Handbook*) – **STOP**: Use Request for Exemption Form available from the IRB Office.

Subjects

1.) Number of subjects/samples/charts to be studied at Bassett (or in local study): 45
(*This number should be justified in the proposal and should include the estimated number that will not qualify after screening or who will otherwise withdraw and not qualify for inclusion in the final data analysis.*)

2.) Category of subjects (*check all that apply*):

☐ Chart review or use of an existing database containing identifiers; no subject contact

☐ Use of preexisting samples only
☒ Patients
☐ Healthy volunteers
☐ Adults (age 18 years or older)
☒ Children (minors below age 18) (*If yes, specify age range and address the following boxes.*) It is generally unacceptable to enroll minors in research trials involving greater than minimal risk where there is no reasonable possibility of direct benefit.

Age Range of Children: 18 months-7 years old

- ☐ A minor's assent statement, in addition to the consent form, is attached to be used by capable minors age 7 & older.
- ☐ A minor's assent statement is incorporated into the consent form to be used by capable minors (generally only applicable to older teenagers).
- ☒ Permission is requested to waive minor's assent (*Justify in the proposal*.)

☐ Females of non-reproductive potential only will be enrolled. *(Justify in the proposal.)*
☐ Females of reproductive potential will be enrolled: *Check one of the following:*

- ☐ The research poses no added risks associated with pregnancy and/or lactation.
- ☐ Precautions against pregnancy and/or lactation, and pregnancy tests, are addressed in proposal and consent form.

☐ Females who are pregnant will be enrolled. *(Provide justification in the research proposal.)*
☐ Individuals who are decisionally compromised will be enrolled. *(It is generally unacceptable to enroll patients unable to give informed consent into research trials where there is no reasonable possibility of direct benefit to the patient resulting from participation.)*

- ☐ Potentially incompetent to give consent due to medical treatment or illness (e.g., ill/injured, sedated, unconscious) *(Justify in the proposal.)*
- ☐ Persons with persistent or permanent cognitive impairment (e.g., mental retardation, alzheimer patients, brain damage) *(Provide justification in research proposal.)*

☐ Prisoner population is targeted (*Provide justification in research proposal. Additional protections are required for this population.)*
☐ Fetus, embryo, fetal material, or *in vitro* fertilization

3.) Type of study *(Check all boxes that apply.):*

☒**Therapeutic** potential (individual subjects may benefit directly from the research intervention)

☒**Randomized** allocation of subjects

☒**Control** group(s) are used: *If yes,* ☒ Placebo control
☐ "Standard-therapy" control
☐ Other control method

☒**Blinded** (masked) study: *If yes,* ☒ Emergency unblinding is permitted

☐**External Sponsor** written research protocol *(submit one copy of sponsor protocol to IRB)*

☐**Multi-center** study *If yes:* Number of subjects at all centers:

☒**FDA regulated** trial *If yes:* Phase of Trial: 4

☐**Observational/Descriptive**

☐**Other**

4.) Data and Safety Monitoring:

Is there a Data and Safety Monitoring Board or similar body that monitors the ongoing research for unexpected adverse events and preliminary results?

Yes ☐ No ☒ Not applicable ☐ (non-interventional or minimal risk study)

(If no, outline in the research proposal how the safety of the subjects and the integrity of research data will be monitored throughout the research.)

The data will be evaluated at the completion of each block of 10 patients by the investigator and statistical group for any safety concerns. The results of these analyses will be reported to the IRB.

5.) ☒ FDA Regulated Items – This research includes items regulated by Food & Drug Administration

If yes, complete the following: (Indicate "pending" if an application is in progress.) Do not list drugs that are being administered as part of usual care. List only those that are investigational. The investigator is responsible for arranging with a registered pharmacist at Bassett Healthcare for the storage, labeling and dispensing of drugs.

Drug or Biologic: Include the **Investigational New Drug (IND)** number, if applicable

- ☒ FDA approved
  - Name(s): Midazolam and xylocaine
  - ☐ Testing new indication for approved item(s) *(If yes, provide name(s) & IND#.)*
    - Name(s) & IND #(s):
- ☐ Non-FDA approved
  - Name(s) and IND #(s):
  - ☐ Investigational Drug Brochure enclosed *(Provide 1 copy with the application.)*
- ☐ Other (explain):

Device: Include the **Investigational Device Exemption (IDE)** number, if applicable

- ☐ FDA approved
  - Names(s) and IDE#(s)
    - ☐ IDE number not required (Justify in the protocol)
- ☐ Non-FDA approved
  - Name(s) and IDE#(s)
    - ☐ IDE number not required (Justify in the protocol)
- ☐ Other (explain):
- ☐ This is a significant risk device
- ☐ This is a non-significant risk device

6.) Health Insurance Portability and Accountability Act (HIPAA) Requirements

The HIPAA Privacy Rule protects individually identifiable health information (Protected Health Information – PHI) in any form, including written, electronic, or oral. The following 18 items are considered identifiers and may not be collected or disclosed for research purposes without authorization from the research subject or other compliance with the HIPAA requirements. Check **all** types of identifiers that will be collected for this research (e.g. on data collection forms, computer databases, case report forms, AE reporting forms, or any other document used specifically for the purposes of this research study).

- ☒ Name
- ☒ Geographic subdivisions smaller than a state (including street address, city, county, precinct, zip code, and their equivalent geographical codes, except for the initial three digits of a zip code in certain situations.)
- ☒ All elements of date (except year) for dates directly related to an individual, including birth date, discharge data, date of death; and all ages over 89 and all elements of dates indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
- ☒ Telephone numbers
- ☐ Fax numbers
- ☐ Electronic mail addresses
- ☐ Social security numbers
- ☒ Medical record numbers
- ☐ Health plan beneficiary numbers
- ☐ Account numbers (for billing purposes)
- ☐ Certificate/license numbers
- ☐ Vehicle identifiers and serial numbers
- ☐ Medical Device Identifiers (e.g., pacemaker)

☐ Web Universal Resource Locators (URLs)
☐ Internet Protocol (IP) address numbers
☐ Biometric identifiers, including finger and voice prints
☐ Full face photographic images and any comparable images
☐ Any other unique identifying number, characteristic, or code

If any boxes are checked above, indicate how you will comply with the HIPAA requirements for this study:

☒ De-identification of Data[1]
☒ Limited data set and compliance with Policy for Access to Protected Health Information for Research[1]
☒ HIPAA Authorization
[Include HIPAA language in consent form(s) or use a stand-alone HIPAA Authorization and specify that subjects will receive a signed copy of the consent/authorization. The HIPAA templates are on the Research Institute IRB website.]
☐ Waiver of Informed Consent (*complete and submit Form D)*

[1] Refer to Bassett Healthcare Policy on Access to Protected Health Information available at http://online2.bassett.org/research/showpage.cfm?pageid=2&pagename=Human%20Subjects%20Research) or on the Bassett intranet under Bassett Research Institute on the Human Subjects Research page under the Policies category.

Will Protected Health Information (PHI) be accessed (used) in the course of prescreening/recruiting for this research?

☒ Yes ☐ No

If "Yes," please complete the Request for Review Preparatory to Research form available at http://online2.bassett.org/research/showpage.cfm?pageid=2&pagename=Human%20Subjects%20Research) or on the Bassett intranet under Bassett Research Institute on the Human Subjects Research page under the Policies category.

7.) Informed consent requirement:

☒ Informed consent will be sought and documented with the attached consent form. *(Approval of the form by the IRB is required.)*
The average educational level of the population Bassett serves is 12th grade, although 20 percent of the adult population has not completed high school. Is the language you are using in your consent form or questionnaire appropriate for the subject population you are dealing with? If yes, please indicate what reading level. (*See page 38 in the Protection of Human Subjects Handbook for a method to estimate reading level.*)

☒ Yes Reading level: 11.9
☐ No If no, describe in question 10 provisions you will make to assure that the subject understands what is being asked.

☐ Request to modify or **waive informed consent** requirement.
(Justify the request in the research proposal. In order to waive consent for projects that involve use of protected health information, also complete and submit Form D.)

☐ Request for waiver of the requirement to obtain signed consent forms.

A. Select **<u>one</u>** of the criteria below and describe how your research meets the selected criteria:

☐ **Criteria 1:** [Typically used for anonymous surveys] The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern:

Or

☐ **Criteria 2:** The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (e.g. sitting down and talking with someone, calling someone at home and asking everyday questions, mall survey, mail survey, internet survey, etc.):

If either Criteria 1 or Criteria 2 above is selected, the IRB suggests that, and may require, the investigator to provide the subjects with a written or verbal statement regarding the research, which should provide subjects with much of the same information that is required within a consent document. This is typically accomplished by providing subjects with an information sheet (i.e., a document similar to a consent form without a request for signature), supplying the information within the invitation letter, or reading the information sheet to the subject over the phone.

B. Will you be providing subjects with a written or verbal statement regarding the research?
☐ Yes [submit supporting document(s) (e.g., information sheet, invitation letter) with this IRB application]

If yes, check all methods that will be utilized to provide subjects with a statement regarding the research:
- ☐ Information sheet physically provided to subjects
- ☐ Information sheet will be read to subjects
- ☐ Information captured within the invitation document
- ☐ Other, describe:

☐ No, provide justification for not supplying subjects with this information.

8.) Recruitment/advertising (check all that apply):

☐ Investigators will **advertise for subjects** *(If yes, include the ad in the application. Approval of the ad by the IRB is required.)* This includes flyers, posters, newspapers, brochures, radio or TV advertisements, internet sites, etc.

☐ Physician-investigators will be recruiting their own patients as participants in this research.
- ☒ Letters will be sent to patients to inform them about the research study. *(Include a copy of the letter in the application. Approval of the letter by the IRB is required.)*

☒ Investigators will be recruiting from active patients under care of other Bassett Healthcare physicians.
- ☐ Letters will be sent to referring physicians to inform them about the research study. *(Include a copy of the letter in the application. Approval of the letter by the IRB is required. Please remember that initial contact with potential participants should be made by their own physician or caregiver.*

☐ Investigator will be recruiting patients from outside physicians.
- ☐ Letters will be sent to referring physicians to inform them about the research study. *(Include a copy of the letter in the application. Approval of the letter by the IRB is required.)*

☐ Investigator will be recruiting patients.

9.) Non-English Speaking Subjects:

Non-English speaking subjects will be included in this study. ☐ Yes ☒ No Not applicable ☐
(*If yes, include the English and the non-English version of all subject documents (i.e., consent forms, written questionnaires, information or recruitment letters.))*

10.) ☒ This project includes a questionnaire/chart audit form/survey

(If yes, include copies with the application)
- ☐ It includes information by which the subject can be identified (e.g., name, medical record number, Social Security number)
- ☐ It includes identifiers and subject matter that is considered sensitive, such as questions related to income, sexual behaviors *(including contraceptive practices)*, use of alcohol, use of illicit drugs, or illegal activities.

If sensitive data is being collected with identifiers, describe (under question 7) provisions you have made for assurance that sensitive information will be protected and if a Certificate of Confidentiality will be used.

11.) ☐ **Biological specimens** will be collected from human participants for research purposes. (*If yes, please check all that apply.)*
- ☐ Specimens are sent to outside laboratory for research tests. *(Address confidentiality issues in consent form.)*

☐ Specimens will be used for genetic studies. *(Address genetic studies in consent form.)*
☐ Specimens will be stored here for future, as-yet-undesignated, research. *(If yes, include tissue options in the consent form and address confidentiality issues in the consent form.)*
If yes, could the future research involve genetic testing? ☐ Yes ☐ No
Explain:
☐ Specimens will be stored at an outside laboratory for future, as-yet-undesignated research. *(If yes, include tissue options in the consent form and address confidentiality issues in the consent form.)*
If yes, could the future research involve genetic testing? ☐ Yes ☐ No
Explain:

A. Are subject-derived biological specimens (fresh human tissue or body fluids) being handled (processed and/or packaged) by individuals who are not hospital employees (i.e., nurses, clinical pathology laboratory personnel)?
☐ Yes* ☐ No

B. Are subject-derived biological specimens (fresh human tissue or body fluids) being handled (processed and/or packaged) in a research laboratory or other setting, other than a licensed Clinical Pathology Laboratory?
☐ Yes* ☐ No

- **If yes to A or B, study personnel handling the specimens must be able to show completion of Bassett Healthcare's Mandatory Education, Section 2, regarding blood borne pathogens and air borne pathogens.**

12.) Research Using Radiation:

A. Will **normal** subjects (i.e., healthy volunteers not being treated or evaluated for an existing or suspected medical condition) be exposed to ionizing radiation (e.g., X-rays, gamma rays, radionuclides) in **any** amount?
Yes ☐ * No ☒

B. Will patients/subjects (i.e., patients being treated or evaluated for an existing or suspected medical condition) be exposed to any type of ionizing radiation in diagnostic procedures, which is not considered standard care (not normally used in such treatment or evaluation)? Yes ☐ * No ☒
Note: this does not apply to therapeutic uses of radiation

***If yes to A or B:** Submit this completed application, consent document and summary of research protocol to the Chairman of the Radiation Safety Committee for approval. Please include a cover letter that includes contact information.

13.) Compensation and/or Financial Responsibilities:

☐ Sponsor has agreed to cover direct costs of treating injuries to subjects.
☐ **Costs:** There may be costs to the subject (or insurer) for the **research**.
If yes, this must be explicitly explained in the consent form.
☐ **Remuneration or reimbursement** will be given to subjects for participation.

If yes, please specify amount or type of remuneration or reimbursement:

Application for Institutional Review Board Approval of Research Involving Human Subjects

Part B - Description of Research

Respond to each of the following items or questions. Provide enough detail so the IRB will be able to judge the importance of the study and the issues related to protection of human subjects.

You must provide a response for each question, numbering to correspond to the question. If not applicable to your study, use N/A.

Specific Aims

1) What is the purpose of this study? What question is it designed to answer?

Primary Objective: To examine the efficacy and tolerability of intranasal midazolam combined with xylocaine as a preoperative sedative in children as compared to intranasal midazolam alone or saline placebo.

Secondary Objectives:

- To examine whether the addition of intranasal xylocaine improves patient acceptance of the intranasal midazolam
- To examine whether the addition of intranasal xylocaine changes the therapeutic effects of intranasal midazolam as measured by sedation scale scores
- To examine whether the addition of intranasal xylocaine effects the length to discharge time

Background

2) Why is this study important?

It has been reported and noted anecdotally that intranasal midazolam when used for preoperative sedation is often poorly tolerated by young children. Agitation due to nasal discomfort and stinging and epistaxis has been reported and observed. Xylocaine is readily available in preoperative settings and is easily obtained for preoperative use. If it is shown to increase patient comfort and increases the acceptance of intranasal midazolam without affecting the sedative effects (positively or negatively), this would be a significant benefit for the preparation of children for mask anesthesia preoperatively. It would also reduce the need to give patients oral medications immediately preoperatively, potentially reducing the risk of aspiration. The intranasal route would also help to ensure more complete delivery of the medication as it is not uncommon for children to expectorate some of the orally administered midazolam.

The pilot project, Project #994, showed no statistical difference in levels of agitation or time to discharge.

Experimental Design and Methods

3) Describe in detail the experimental design and methodology. What information will be collected and how will it be collected? Provide a description of the subject's participation from start to finish.

This will be a double blind, randomized, placebo controlled study. Study participants will be children ages 18 months-7 years scheduled for minor otolaryngeal (ENT) surgical procedures requiring mask anesthesia.

Study participants will be randomly assigned to one of three treatment groups:

- Group 1 – Placebo – Control patients will receive intranasal saline.
- Group 2 – Nasal Midazolam Only – Patients will receive 0.2 mg/kg of intranasal midazolam.
- Group 3 – Midazolam Plus Xylocaine – Patients will receive 0.2 mg/kg intranasal midazolam plus xylocaine 4% in a dose based on 50% of the volume of the midazolam.

The volume of the study medications will be shielded from the investigators and the administering staff. All study medication will be administered into a single nares using an atomizer commonly used in the OR. The following assessments will be completed:

- Verbalized complaints will be recorded by the administering RN at time of administration, at 1 minute, and 5 minutes post-administration.
- Any episodes of epistaxis will be recorded.
- The administering RN and 1 accompanying parent will complete the Observed Behavioral Distress (OBD) VAS at 1 minute and 5 minutes post administration.
- The administering RN will complete the Sedation scale at 10 minutes and 15 minutes post administration.
- The CRNA/MDA will complete the sedation scale at the time of transport to the OR and at time of induction of anesthesia.

- The time to discharge from the Post Anesthesia Care Unite (PACU) to the Ambulatory Surgery Unit (ASU) will be recorded.
- The time to discharge from ASU to home will be recorded.

4) If the research is in part a treatment protocol, identify which parts are routine and which parts are being done solely for research.

Preoperative sedation with midazolam using the intranasal route is a common practice. The addition of xylocaine or the like is done in some practices, but is not as common as the use of midazolam alone or the exclusion of preoperative sedation all together. The use of a placebo is for research purposes only.

Human Subjects

5) Identify the inclusion and exclusion for subjects.

Inclusion Criteria:

1. Children aged 18 months-7 years, scheduled for a minor ENT surgical procedure requiring mask anesthesia
2. American Society of Anesthesiologists (ASA) Class 1 or 2
3. Parent willing and able to provide written informed consent
4. Parent willing and able to complete the OBD VAS

Exclusion Criteria:

1. ASA Class 3 or greater
2. History of allergy to midazolam or xylocaine
3. Presence of acute respiratory infection at time of surgery
4. Parent unwilling or unable to provide informed consent
5. Parent unwilling or unable to complete the OBD VAS

6) Are there enrollment restrictions based on race, gender or age? If yes, specify the restriction and provide justification for the restrictions.

Only children (male or female) ages 18 months-7 will be eligible.

7) How will subjects be identified, recruited, or otherwise enlisted to participate?

Subjects will be referred by the surgeon performing the planned surgery or they will be identified from the surgery schedules by the investigator or research staff.

Risks/Discomforts and Safeguards

8) Describe all reasonably foreseeable risks and discomforts, including their likelihood and seriousness and identify the safeguards that will be used to minimize risk. Likelihood should be quantified whenever possible. Types of risk include: physical, psychological, social, legal, or other risks. Include the risks associated with any drugs or procedures that are used or performed solely for research (e.g., x-rays, anesthesia, and surgery). Do not include risks that are part of usual care.

The most common risks for intranasal midazolam are minor and include stinging, burning, epistaxis, and crying. Respiratory depression is possible but rare.

Describe alternative procedures that might be advantageous (lower risk) to the subjects (when appropriate).

A commonly used alternative route for midazolam is oral, although there is a risk of drug loss through expectoration and potential risk for aspiration.

Describe procedures for protecting against or minimizing potential risk to subjects. Describe confidentiality safeguards. If Protected Health Information is being used, identify who will have access to this information.

All patients will be observed and monitored per usual conscious sedation and anesthesia protocols. All study documents, including any that may contain PHI, will be stored in the Clinical Research Division in a locked office with limited access. Study information used for data analysis and possible publication will be de-identified.

Describe provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects.

Appropriate nursing and anesthesia staff and equipment will be available at all times to treat any adverse events that might occur.

Risk/Benefit Assessment

9) Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects, or the anticipated benefits to society.

Risks are minimal based upon literature review and anecdotal experience. Even the oral route of midazolam administration may be accompanied by crying and agitation immediately following drug administration. The known side effects of intranasal midazolam as noted above are minor and short lived, rarely requiring intervention. If the addition of xylocaine improves patient comfort and acceptance of the intranasal route of administration it can be readily administered without relying on a patient to swallow the drug, ensuring more complete delivery without the theoretical risk of aspiration of gastrointestinal contents that may be associated with the oral route of administration.

Compensation

10) Describe any payments or compensation (financial or non-financial) to subjects and the schedule and conditions to receive them.

There is no financial compensation for subjects.

Informed Consent

11) How will you obtain informed consent of the subjects? What will be the setting? Who will approach the subject? How long will they have to decide whether to participate? What will be your criteria for assuring that the subject understands what his/her participation means?

Informed consent will be obtained from the patient's parent or legally authorized representative (LAR). Initial introduction of the study to the parents/LAR will be by the operating surgeon. Research staff will review the study details and plan, and obtained the written informed consent from the Parent/LAR. Parents/LAR will have ample time to review the written material and to ask questions of the physicians and research staff. They will have up until the time of surgery to decide if they agree to allow their child to participate. Research staff are trained in and experienced in administering the informed consent and eliciting evidence of understanding.

Investigators

12) Identify all personnel involved in this study, their roles on the study *(also include, as applicable, the following options - study conduct, recruitment, obtaining informed consent, data analysis, and manuscript preparation)* and qualifications. Note most recent date they have completed IRB training.

Name	Role	Qualifications	Most recent date of IRB training
David Ullman, MD	Principal Investigator – study conduct, recruitment, data analysis, manuscript prep	**Attending Physician - Anesthesiology**	**09/14/14**
Jennifer Victory, RN, CCRC	**Study Coordinator – recruitment, informed consent, drug administration, data collection**	**Clinical Research Nurse Supervisor**	**09/05/14**
Catherine VanWarner, RN, CCRC	**Research Nurse - recruitment, informed consent, drug administration, data collection**	**Clinical Research Nurse Facilitator**	**04/02/14**
Julie Tirrell, RN	**Research Nurse - recruitment, informed consent, drug administration, data collection**	**Clinical Research Nurse Facilitator**	**01/20/14**

References

13) If available, provide references to published material that might help the committee assess the possible risks and benefits associated with this protocol.

Bjorkman, S., Rigemar, G., Idvall, J. (1997). Pharmacokinetics of midazolam as an intranasal spray to adult surgical patients. *British Journal of Anaesthesia*. **79**: 575-580.

Karl, H., Rosenberger, J., Larach, G., Ruffle, J., (1993). Transmucosal administration of midazolam for premedication of pediatric patients: Comparison of nasal and sublingual routes. *Anesthesiology*. **78**(5): 885-891.

Bhakta, P., Ghosh, B., Roy, M., Mukherjee, G., (2007). Evaluation of intranasal midazolam for preanasthetic sedation in paediatric patients. *Indian Journal of Anesthesiology*. **51**(2): 111-116.

Karl, H., Keifer, M., Rosenberger, J., Larach, G., Ruffle, J., (1992). Comparison of the safety and efficacy of intranasal midazolam or sufentanil for preinduction of anesthesia in pediatric patients. *Anesthesiology.* **76**:209-215.

McCann, M., Zeev, N. (2001). The management of preoperative anxiety in children: An update. *Anesthesiology & Analgesia.* **93**(1): 98-105.

Sedation: Intranasal sedatives. *Therapeutic Intranasal Drug Delivery: Needleless treatment options for medical problems.* Retrieved from : http://intranasal.net/Sedation/default.htm.

ATTACH CONSENT FORM