Title: Is end tidal CO2 level elevation during upper endoscopy with CO2 gas insufflation physiologically significant?

NCT Number: NCT04541667

Document Date: 6/3/2021

Biomedical
SECTION I

Therapeutic/Non-Therapeutic
Does your research involve a drug, medical device, technique or other intervention or strategy (including means like diet, cognitive therapy, behavioral therapy, exercise) to diagnose, treat or prevent a particular condition or disease: "THERAPEUTIC RESEARCH"?
Yes

1. Title of Protocol:
Is end tidal CO2 level elevation during upper endoscopy with CO2 gas insufflation physiologically significant?

2. Responsible Personnel:
A. Principal Investigator (PI):
Dike, Chinenye R - Pediatrics Gastroenterology - 402-955-5150 - chinenye.dike@unmc.edu - alt #: 402-955-5710 - degree: MBBS - address: CHMC-IHE 8200 Dodge Street, IHE6 (Zip 2155) - phone: 402-955-5150

B. Secondary Investigator (SI):
Huang Pacheco, Andrew Steve S - Pediatrics Gastroenterology - 402-955-5700 - a.huangpacheco@unmc.edu - alt #: 612-800-1627 - degree: MD - address: CHMC-IHE 8200 Dodge Street, IHE6 (Zip 2155) - phone: 402-955-5700

Shukry, Mohanad - Anesthesiology - 402-955-4385 - mohanad.shukry@unmc.edu - alt #: 402-955-8581 - degree: MD/NE - address: BTH 2017 UNMC Midtown (68114-4455) - phone: 402-955-4385

C. Participating Personnel:
Choudhry, Ojasvini C - Pediatrics Gastroenterology - 402-955-5700 - ojasvini.choudhry@unmc.edu - alt #: 402-305-5484 - degree: MBBS - address: CHMC-IHE 8200 Dodge Street, IHE6 (Zip 2155) - phone: 402-955-5700

Freestone, David J - Pediatrics Gastroenterology - 402-955-5718 - david.freestone@unmc.edu - alt #: 801-309-0615 - degree: DO - address: CHMC-IHE 8200 Dodge Street, IHE6 (Zip 2155) - phone: 402-955-5718

Kusek, Mark Edward - Pediatrics Gastroenterology - 402-955-5712 - mkusek@unmc.edu - alt #: 402-955-5712 - degree: MD - address: CHMC-IHE 8200 Dodge Street, IHE6 (Zip 2155) - phone: 402-955-5712

Lyden, Elizabeth Ruby - COPH Biostatistics - 402-559-6061 - elyden@unmc.edu - alt #: 402-559-6061 - degree: MS - address: MCPH 3046 UNMC Midtown (Zip 4375) - phone: 9-6061

Quiros, Ruben E - Pediatrics Gastroenterology - 402-559-8968 - rquiros@unmc.edu - alt #: 402-955-5400 - degree: MD - address: UT1 5135 UNMC Midtown (Zip 2161) - phone: 9-8968

D. Lead Coordinator:
Roberts, Evan Michael - Child Health Research Institute - 402-836-9742 - evan.roberts@unmc.edu - alt #: 402-547-1954 - degree: MBA, BS - address: CHMC-IHW 8200 Dodge Street, IHW5 (Zip 5456) - phone: 402-836-9742

E. Coordinator(s):
Abraham, Kym L - CHRI Administration - 402-559-2977 - kabraham@unmc.edu - alt #: 402-559-2977 - degree: RN, BSN - address: CHMC-IHW 8200 Dodge Street, IHW5 (Zip 5456) - phone: 9-2977

Hoover, Denise M - CHRI Administration - 402-559-0686 - dmhoover@unmc.edu - alt #: 402-559-0686 - degree: BS - address: CHMC-IHW 8200 Dodge Street, IHW5 (Zip 5456) - phone: 9-0686

F. Data/Administrative Personnel:
Fischer, Laura Jean - CHRI Administration - 402-836-9762 - laura.fischer@unmc.edu - alt #: -- - degree: MPH - address: CHMC-IHW 8200 Dodge Street, IHW5 (Zip 5456) - phone: 402-836-9731

Servais, Ashley Nicole - CHRI Administration - 402-559-2511 - ashley.servais@unmc.edu - alt #: 402-559-2511 - degree: MPH - address: CHMC-IHW 8200 Dodge Street, IHW5 (Zip 5456) - phone: 9-2511

G. Are you a student or house officer?
No

3. Funding Source:
Check all that apply and provide the source of the funding.
Cooperative Group:
Center for Clinical and Translational Research (CCTR)
Federal (e.g., NIH) Grant - Provide source:
♦ Other Grant: Diversity and Inclusion Grant UNMC
Departmental funding
Commercial - Provide company name:
Department of Defense
Other - Provide source (e.g. personal funding):

4. Deadline for IRB Approval:
Yes - Explain and provide date:
♦ No

5. Contract:
Is there a contract associated with this study?
No

6. Agreements
Is there a Material Transfer Agreement (MTA) associated with this study?
No

Is there a Data Use Agreement (DUA) associated with this study?
No

Is there a Data Transfer Agreement (DTA) associated with this study?
No

7. Study Sites:
A. Provide the names and locations of all study sites where this research will be conducted under the oversight of the UNMC IRB or Joint Pediatric IRB.
CHMC

B. Will the research be conducted at external sites under the oversight of an external IRB?

No

C. Does UNMC, TNMC, CHMC or UNO serve as the lead site with responsibility for data and/or safety monitoring?
No

D. Does this study involve any international sites where the PI will either; 1) conduct 2) supervise or 3) receive / ship HBM or data to / from UNMC?
No

8. Principal Investigator Assurance
The PI understands and accepts the following obligations to protect the rights and welfare of research subjects in this study:
I certify that:

- **I have carefully reviewed this application and all supporting documents. I have determined that the application is accurate, complete and ready for submission to the IRB.**
- **I, and all listed research personnel, have the necessary qualifications, expertise, and hospital credentials to conduct this study in a manner which fully protects the rights and welfare of research subjects.**
- **There are, or will be, adequate resources and facilities to safely initiate, carry out and complete this research at the study sites specified in Section I.7. This includes sufficient staff, funding, space, record keeping capability, and resources necessary to address adverse events and any unanticipated problems involving risk to the subject or others. If the necessary resources become unavailable I will promptly notify the IRB.**
- **All listed research personnel, including external investigators, will be given a copy of the final IRB approved application and any other relevant study-related documents in accordance with their defined responsibilities.**
- **All listed research personnel, including external investigators, will be notified promptly of any changes in protocol, in accordance with their defined responsibilities.**
- **Research personnel, including data and administrative personnel who have access to protected health information (PHI) or subject identifiers will have adequate training in confidentiality and protection of PHI.**
- **The minimum amount of protected health information (PHI) or other identifiers necessary will be used and disclosed to conduct this research study (if applicable). I will implement reasonable safeguards to protect the PHI/identifiers at all times.**
- **I and all other personnel listed in Section I.3A-E of the IRB Application have**

disclosed all potential financial conflicts of interest as required and are in full compliance with the UNMC Conflict of Interest Policy #8010 and HRPP Policy. I further certify that all potential financial conflicts of interest are appropriately managed in order to ensure protection of the rights and welfare of subjects.

I recognize that:

- As the PI it is my responsibility to ensure that this research and the actions of all research personnel involved in conducting the study will comply fully with the IRB-approved protocol (including all amendments), all applicable federal regulations, state laws, and HRPP policies.
- It is my responsibility to ensure that valid informed consent/assent will be obtained, as appropriate, from all research subjects or their legally authorized representative(LARs).

I will:

- Ensure that all research personnel involved in the process of consent/assent are properly trained and are fully aware of their responsibilities relative to the obtainment of informed consent/assent according to federal regulations, state laws, and HRPP policies.
- Promptly inform the IRB of internal adverse events, as well as any unanticipated problems involving risk to the subjects or to others, as required within the time frame defined by HRPP policies. I will analyze each internal adverse event/reported problem to determine if it impacts the risk-benefit relationship of the study, the safety of the subjects, or informed consent.
- Analyze each MedWatch/safety report to determine if it impacts the risk/benefit relationship of the study, the safety of the subjects, or informed consent.
- Promptly submit external adverse event reports in accordance with HRPP policies.
- Promptly inform the IRB if I become aware of 1) any complaints from research subjects, LARs, or others about research participation, 2) violations of federal regulations or state law, 3) violations of the HIPAA Rule, or 4) violations of HRPP policies.
- Promptly inform the IRB of the results of external audits performed by sponsors, Contract Review Organizations (CROs), cooperative groups, FDA, or other external groups.
- Not initiate any change in protocol without IRB approval except when it is necessary to reduce or eliminate a risk to the subject, in which case the IRB will be notified as soon as possible.
- Promptly inform the IRB of any significant negative change in the risk/benefit relationship of the research as originally presented in the protocol and approved by the IRB.
- Maintain all required research records on file and I recognize that

representatives from the IRB, OHRP, HHS, FDA, and other Federal Departments or Agencies may inspect these records in accordance with granted authority.

I understand that:

- **Continuing review by the IRB is required at least annually, or as per Federal Regulations and HRPP Policy, in order to maintain approval status. I will maintain IRB approval as long as this study is active.**
- **I am responsible for appropriate research billing in accordance with UNMC Clinical Trial Professional and Technical Fee Billing Policy #8008 or applicable Children's Hospital & Medical Center policy.**

Failure to comply with the Common Rule, applicable Subparts B, C, and D of HHS regulations at 45 CFR 46, applicable FDA regulations, the HIPAA Rule, applicable state law, HRPP policies, and the provisions of the IRB-approved protocol may result in suspension or termination of IRB Approval of my research project and/or other administrative or legal actions.

Dike, Chinenye R - 2021-01-31 08:48:34.423

9. Principal Investigator Financial Interest Disclosure

A. As the PI, I declare:

♦ I have no financial interest in this research.

I have a financial interest in this research.

B. As the PI, I understand

♦ I must disclose any change in my financial interest during the course of this research within five (5) business days from the time the change becomes known.

C. As the PI, I certify that:

♦ No Responsible Personnel have a financial interest in this research.

The Responsible Personnel listed below have informed me that they have a financial interest in this research.

D. I have informed all Responsible Personnel that if there is any change in their financial interests during the course of this study it must be disclosed within five (5) business days from the time the change becomes known.

Dike, Chinenye R - 2021-01-31 08:48:34.423

11. Scientific/Scholarly Merit and Resource Review Certification

Scientific Reviewer:

Rizzo, William Bradley - Pediatrics Metabolism - 402-559-2560 - wrizzo@unmc.edu - alt #: 402-559-2560 - degree: MD - address: DRC2 4064 UNMC Midtown (Zip 5940) - phone:

9-2560

As the Scientific Reviewer,
♦ I do not have a financial conflict of interest associated with this study.
I do have a financial conflict of interest associated with this study.

My signature certifies that:

- **this application has been reviewed for scientific/scholarly merit and available resources. It has been determined that the application merits consideration by the IRB based upon the following:**
- **The proposal has an acceptable level of scientific/scholarly merit which justifies the involvement of human subjects.**
- **The proposal has a sound research design in consideration of the stated objectives,**
- **The PI has the necessary qualifications, experience and credentials to conduct this research.**
- **The PI has or will have the necessary funding to support this research**
- **There is or will be adequate physical space required for the research interventions at all study sites specified in Section I.7. In addition, there is or will be adequate laboratory and administrative support, data storage capability, and any other resources necessary to complete this research.**
- **At all study sites specified in Section I.7, there is or will be emergency equipment, personnel, or services necessary to respond promptly to adverse events or unanticipated problems involving risk to the subject or others.**
- **I will promptly notify the IRB if the necessary resources to support this research become unavailable.**

Rizzo, William Bradley - 2019-08-14 10:57:00.000

SECTION II

PROTOCOL ABSTRACT

1. Provide a brief (less than 2500 characters) abstract of the research protocol. (2500 characters)
This summary should include: 1)) a brief description of the purpose of the study, 2) eligibility criteria, 3) interventions and evaluations and 4) follow-up.

Luminal inflation is essential for adequate visualization and endoscope advancement during endoscopy. Although air has previously been the standard gas used, CO2 is increasing preferred in adult endoscopy centers, due to reports of decreased post-procedural abdominal discomfort compared to air. Few published studies in children demonstrated decreased abdominal discomfort with use of CO2, but safety concerns for its use in pediatric endoscopy remain. During my fellowship, I conducted a randomized, double-blinded study comparing the safety and efficacy of CO2 and air for all procedures. This study showed that CO2 use for insufflation in pediatric upper endoscopy was associated with multiple transient elevations in end-tidal CO2, in non-intubated patients. It is important to investigate whether the observed elevations in end-tidal CO2 may be actually absorbed or just eructated. Therefore, with this study we plan to: (I) compare the end tidal CO2 levels observed during upper endoscopy in children managed with endotracheal intubation or laryngeal mask airway using CO2 versus air and compare how these levels deviate from the pre-procedure baseline levels. (ii) Observe whether there are particular pre-procedural risk factors that predispose children to hypercapnia with CO2 use during upper endoscopy. (iii) Determine if carbon dioxide gas use for insufflation results in significant changes in the minute ventilation. This is a Double-blinded, prospective, randomized study of all pediatric patients undergoing procedures involving upper endoscopy in the Childrens Hospital & Medical Center. Children from 6 months to 19 years of age undergoing upper endoscopy related procedures. Randomization will for intubated patients who require an advanced airway (endotracheal intubation or laryngeal mask airway) 1:1 for air or CO2. Risks assessed before the procedure will include past medical history, American Society of Anesthesiology (ASA) classification. Vital signs will be recorded before the procedure, throughout the procedure and after the procedure until fully awake. While in the procedure room, end-tidal CO2 level and minute ventilation (tidal volume X RR) will be continuously recorded. Patients and legal guardians who decline participation in the study and patients with chronic respiratory disease (defined as severe asthma, bronchopulmonary dysplasia and CF related pulmonary disease), cyanotic heart disease and ASA status >/= 3 will be excluded from the study.

PURPOSE OF THE STUDY AND BACKGROUND

2. Purpose of the Study

What are the specific scientific objectives of the research?
(I) Compare the end tidal CO2 levels observed during upper endoscopy in children managed with endotracheal intubation or laryngeal mask airway using CO2 versus air and compare how these levels deviate from the pre-procedure baseline levels.
(ii) Observe whether there are particular pre-procedural risk factors that predispose children to hypercapnia with CO2 use during upper endoscopy.
(iii) Determine if carbon dioxide gas use for insufflation results in significant changes in the minute ventilation

3. Background and Rationale
Describe the background of the study. Include a critical evaluation of existing knowledge, and specifically identify the information gaps that the project is intended to fill.
Luminal inflation is crucial for proper visualization and advancement of the endoscope during endoscopy (2). Air has been the standard insufflation gas during endoscopy. However, multiple adult studies have demonstrated decreased abdominal discomfort and increased efficacy with carbon dioxide (CO_2) use (3-9). Therefore, many adult endoscopy centers now use carbon dioxide routinely for endoscopy insufflation. Only 3 pediatric studies exist on the use of CO_2 for colonoscopy (10-12). Two of these studies demonstrated that CO_2 use was associated with decreased abdominal discomfort after colonoscopy. During my fellowship, we showed, through a recent survey of fellow trainees across North America, that though air remains the predominant gas for insufflation during endoscopy in pediatrics, CO_2 is increasingly being used. We have also demonstrated through our study that CO_2 use during upper endoscopy in children is associated with significant elevations in end-tidal CO_2 levels. This finding is likely the result of eructated CO_2 used during in upper endoscopy, as most of the patients in our study did not have the airway isolated by intubation. It is also possible that there is excessive direct absorption of CO_2 from the upper GI tract. This study has been written up and the manuscript is awaiting editorial decision. It has been presented at a national conference (Digestive Disease Week, San Diego; May 2019). In a follow up study, CO_2 use during upper endoscopy was not associated with significant elevations in transcutaneous CO_2 level.

We hypothesize that transient elevations in end tidal CO_2 level observed with CO_2 use during upper endoscopy is due to eructation of the instilled gas and will be eliminated by protection of the airway. We also hypothesize that there will be no changes in minute ventilation associated with CO_2 use during upper endoscopy in patients who are intubated (via endotracheal tube or laryngeal mask airway).
**Amendment- We will now enroll 19 year old's (Adults) into this study and also Spanish Speaking subjects.

CHARACTERISTICS OF THE SUBJECT POPULATION

4. Accrual
A. Is this study conducted solely at sites under the oversight of the UNMC IRB (e.g. UNMC, Nebraska Medicine, CHMC, UNO)?
Yes

1. How many subjects will need to be consented (per group, as applicable) in order to achieve the scientific objectives of the research?
230 subjects total (100 each group). This extra 30 subjects will allow for screen failures that occur on the study for example change in plans from use of ETT or LMA to nasal cannula in the procedure room after subjects may have been consented. They will not be randomized and need to be replaced on the study.

2. What is the statistical or other justification for the total number of subjects described above?
Sample sizes of 75 per group achieve 80% power to detect a difference of 2 mmHg between the null hypothesis that both group mean EtCO2 measurement over the length of the monitoring period are 37.2 mmHg and the alternative hypothesis that the mean of the CO2 group is 39.2 with an estimated within group standard deviation of 4.3 mmHg and with a significance level (alpha) of 0.05 using a two-sided two-sample t-test. To adjust for the possibility of a 25% drop out rate 100 patients per group will be enrolled.

We have also allowed 30 extra subjects due to some screen failures we have had.

5. Gender of the Subjects
A. Are there any enrollment restrictions based on gender?
No

6. Age Range of Subjects
A. Will adults be enrolled ?
Yes

1. What is the age range of the adult subjects?
The adults in this study will be 19 years old.

2. What is the rationale for selecting this age range?
As we were enrolling subjects into this study we noticed we had several 19 year old subjects still being seen by our GI Department. Therefore, they would qualify for the study. We did

not want to exclude them from participating in the study. The research will be conducted in children aged 6 months to 19 years to determine if end tidal CO_2 remains persistently elevated in intubated children undergoing upper endoscopy with CO_2 insufflation and to determine if there are changes in minute ventilation with CO2 use during upper endoscopy.

B. Will children (18 years of age or younger) be included in this research?
Yes

1. What is the justification for inclusion of children in this research?
The research will be conducted in children aged 6 months to 18 years to determine if end tidal CO_2 remains persistently elevated in intubated children undergoing upper endoscopy with CO_2 insufflation and to determine if there are changes in minute ventilation with CO2 use during upper endoscopy.

2. What is the age range for the child subjects, and what is the justification for selecting this age range?
6 months to 18 years. The justification for this age range is that carbon dioxide is increasingly used for insufflation in pediatric endoscopy. Though there is an increase in its use, the deleterious effects of carbon dioxide insufflation and absorption in this age group are not known. This highlights the importance on further studies in this age group to determine if this elevated end tidal CO_2 level can be avoided by intubation, if there are changes in the minute ventilation with CO2 use and if it is physiologically significant and should be used with caution.

3. Will this study enroll wards of the state?
No

7. Race and Ethnicity
Are there any subject enrollment restrictions based upon race or ethnic origin?
No

8. Vulnerable Subjects
A. Will prisoners be included in the research?
No

B. Select from the list all of the vulnerable populations that will specifically be recruited to participate in this research.
Decisionally-impaired persons
Critically ill patients

Students of the investigator
Employees of the investigator
Educationally disadvantaged individuals
Socially or economically disadvantaged individuals
Individuals with a stigmatizing illness or condition
Individuals from a marginalized social or ethnic group
Other.
♦ No vulnerable subjects will be specifically recruited

9. Inclusion Criteria
What are the specific inclusion criteria?

- Children 6 months to 19 years old undergoing upper endoscopy in CHMC whose parents or legal guardians consent to the study will be included.

10. Exclusion Criteria
What are the specific exclusion criteria?

- Patients and legal guardians who decline participation in the study and patients with chronic respiratory disease (defined as severe asthma, bronchopulmonary dysplasia and cystic fibrosis related pulmonary disease) will be excluded from the study. Patients with cyanotic heart disease and those with ASA status of ≥ 3.
- Patients who are wards of the state or in foster care will be excluded as well
- Prisoners will be excluded
- Patients undergoing colonoscopy only procedures or procedures not related to upper endoscopy will be excluded

11. Pregnancy and Contraception Requirements
A. Are women of child bearing potential (WOCBP) included in this research?
Yes

a. Are there any specific contraception requirements for subjects?
No

1. Provide justification for absence of contraception requirements
There are no interventions that are likely to be of risk to a fetus
Investigational drug(s) is (are) not systemically absorbed
Investigational drug(s) is (are) systemically absorbed, but there is no evidence from human studies, or from clinical experience, that there is risk to a fetus
♦ Other Patients undergoing endoscopic procedures under anesthesia are already being screened for pregnancy as per CH&MC pre-surgical protocol. This study does not pose any

other risks to the fetus besides the risk of anesthesia

B. Are pregnant women included in this research?
No

1. Provide justification for excluding pregnant women
Investigational drug(s) is (are) absorbed systemically, and there is evidence from animal or human studies, or from clinical experience, that there is risk to a fetus **OR** investigational drug(s) is (are) absorbed systemically, and there is a well-understood mechanism of action that may result in risk to a fetus
Intervention includes a procedure expected to be of risk to a fetus (eg, exposure to ionizing radiation, maximal exercise test)
Research is not relevant to pregnant women (e.g. disease or condition rarely encountered in pregnant women)
Knowledge being sought in the research is already available for pregnant women or will be obtained from another ongoing study
A separate study in pregnant women is warranted and preferable
Physiology of pregnancy precludes generalization to other populations
♦ Other - explain There is risk of anesthesia to the developing fetus. Therefore, pregnant women are rarely scheduled for elective procedures unless the benefits of the procedure outweigh the risks

2. Describe how pregnancy status will be assessed (eg, self-report, urine pregnancy test, blood pregnancy test) and the frequency of monitoring during participation in the research.
A CHMC pre-surgery nurse asks the WOCBP if she could be pregnant. If the answer is no, they move forward with the procedure. If the answer is yes or they are unsure then a urine pregnancy test is done as per anesthesia protocol prior to an elective procedure due to risk of anesthesia to the fetus. Therefore a routine monitoring of pregnancy status will be done whether the subject is participating in the study or not.

3. Describe the plan should a female subject, or the partner of a male subject, become pregnant while research interventions are on-going (or during the period that contraception is required following the completion of the intervention).
The study only occurs during the procedure and therefore, investigators will not require female subjects or partners of male subjects to provide information if they become pregnant after the procedure/ study completion.

C. Are breast feeding women excluded from participation?

No

METHODS AND PROCEDURES

12. Methods and Procedures Applied to Human Subjects
A. Are there any evaluations or tests that will be performed for the purpose of determining subject eligibility which would not be routinely conducted as part of standard clinical care of the prospective subject?
No

B. Describe the research plan, including all procedures, interventions, evaluations and tests.
This is a double blinded prospective randomized study of pediatric patients undergoing procedures involving upper endoscopy in Childrens Hospital of Omaha.

- Children from 6 months to 19 years of age who meet the inclusion criteria would be approached for enrollment.
- Consent will be obtained and signed by all legal guardians or parents
- A verbal explanation of the study will be done to all children who are 7 years of age and neuro developmentally appropriate up to age 12 and verbal assent will be obtained by children who agree to participate in the study.
- Children who are 13 years to 19 years of age will be required to sign the consent form with their parents or legal guardians if they are willing to participate in the study.
- Patients will be randomized 1:1 for air and CO_2 using a card system by the endoscopy room/procedure nurse.
- The procedure room/ endoscopy room nurse will then randomize the patients as described below:
  The nurse will receive 4 envelopes.
  Each envelope will contain 25 cards marked "Air" and 25 cards marked "CO_2;
  Therefore, there will be a total of 100 cards marked "Air" and 100 cards marked "CO_2" in all the 4 sets of envelopes
  After it has been determined that the patient can be included in the study and the consents have been signed; the procedure nurse will open the first envelope and randomly pick either CO_2 or Air. She will then set up the insufflation gas based on the gas picked. She will cover the air and CO2 dispensing machine so that the patient, anesthesiologist and endoscopist are all blinded to the type of insufflation gas used during the procedure. She will complete randomization using the cards in each set of envelope before moving to the next set. The endoscopy room/procedure room nurse will keep a record of patients randomized into the air or CO_2 group in a locked cabinet. She will assign arbitrary letters or numbers to the gas used so that the biostatistician who will perform the interim analysis will be blinded to the arm of

study as well.

- Data including age, gender, weight z scores, BMI, co-morbid factors and reason for endoscopy will be collected on all children enrolled in the study. Name and level of expertise of the endoscopist will be collected including the duration of both the procedure and anesthesia and any procedural or anesthesia related complications encountered during the procedure or within forty-eight hours of the procedure.
- Vital signs including heart rate, respiratory rate, blood pressure, end tidal CO_2 level and minute ventilation (tidal volume x respiratory rate) will be recorded before the procedure and continuously monitored during the procedure as per anesthesia protocol.
- Information regarding end tidal CO_2 level and minute ventilation will be recorded for both groups and compared to the pre-procedure values. We will also collect data on the type of anesthetic medications used and the presence of any of these symptoms (nausea, vomiting or headaches) after the procedure. Please also see attached flow chart below for protocol and randomization.

C. Select any of the following that apply to the research:

Phase I study
♦ Randomization
Placebo (or non-treatment arm)
Washout
Sensitive surveys or questionnaires
None of the above

Describe randomization process and schedule

This is a double blinded , randomized clinical study. Both the endoscopist and patients will be blinded to the insufflation gas used; Air or CO_2. The procedure room/ endoscopy room nurse will then randomize the patients as described below:
The nurse will receive 4 envelopes.
Each envelope will contain 25 cards marked "Air" and 25 cards marked "CO2" ; Therefore, there will be a total of 100 cards marked "Air" and 100 cards marked "CO2" in all the 4 sets of envelopes
After it has been determined that the patient can be included in the study and the consents have been signed; the procedure nurse will open the first envelope and randomly pick either CO2 or Air. She will then set up the insufflation gas based on the gas picked. She will cover the air and CO2 dispensing machine so that the patient, anesthesiologist and endoscopist are all blinded to the type of insufflation gas used during the procedure. She will complete randomization using the cards in each set of envelope before moving to the next set. The endoscopy room/procedure room nurse will keep a record of patients randomized into the air or CO2 group in a locked cabinet. She will assign arbitrary letters or numbers to the gas

used so that the biostatistician who will perform the interim analysis will be blinded to the arm of study as well.
We will perform an interim analysis after enrolling 100 patients (50 patients in the Air group and 50 patients in the CO2 group)

D. Identify:
1. All procedures, interventions, evaluations and tests performed solely for research purposes (eg, administration of an investigational drug or a new psychological assessment instrument; randomization)
The consenting process for the study is only done for research purposes. Also, the only other procedures that would be performed solely for research purposes is the randomization of enrolled patients to air or CO_2 gas for insufflation during the endoscopic procedure. Although, air is the standard insufflation agent for endoscopy in pediatrics; many centers now routinely use carbon dioxide given the vast data in adults showing decreased abdominal discomfort and distension with carbon dioxide use.
In our center, we routinely use CO_2 for colonoscopy and most endoscopists use air for upper endoscopy.

2. All procedures, interventions, evaluations and tests performed for clinical indication but more frequently than they would be if the subject was not participating in the research (eg, extra blood tests; additional radiology exams)
There will be no extra blood tests or additional radiology exams

E. Describe briefly the statistical methods used to analyze the data (or reference the appropriate section of the detailed protocol or grant).
Continuous data will be reported as means with standard deviations, or medians with interquartile ranges depending if variable has normal or skewed distribution respectively. Categorical variables will be described by percentages and proportions. Comparisons of continuous data will be performed using the t-test or Wilcoxon signed-ranks test. Categorical variables will be compared using the chisq test or Fishers exact test. A probability value <.05 will be considered significant. Statistical analysis will be performed using SAS 9 statistical software (SAS Institute, Cary, NC) or Graph Pad Prism 7 for Windows (Graph pad Software, San Diego, CA).
Descriptive statistics, including counts and %, means, SD, medians, will be used to summarize patient characteristics, procedural, anesthesia and safety outcomes for the two groups. Patient characteristics, Patient safety outcomes;(MV, $EtCO_2$), procedural, and anesthesia outcomes will be compared between the groups using the independent sample t-test or Mann-Whitney test or Fishers exact test as appropriate to the data. Changes in these safety outcome measurements across the monitoring period between the two groups using a mixed effects model will be considered

F. Does this study involve the collection of blood, urine, saliva or other human biological material (HBM)?
No

DRUGS, BIOLOGIC DRUGS AND DEVICES

13. Drugs and Biologic Drugs
1. Does this research involve the use of drugs or biologics?
No

14. Devices
1. Does this research involve a medical device(s)?
No

CONFIDENTIALITY AND PRIVACY

15. Confidentiality and Privacy
A. Describe where research data will be stored. Check all that apply.
♦ On a secure server at UNMC, CHMC, Nebraska Medicine, and/or UNO (including REDCap)
On a secure cloud server - Specify the secured cloud serve:
On a firewall protected database accessible through the internet - Specify who has administrative responsibility for maintenance of the server:
On an encrypted, password protected local hard drive
On an encrypted, password protected portable computer
On an encrypted, password protected flash drive
♦ In hard copy
♦ Other Hard copies of the original signed consent and assent forms will be stored in a locked file cabinet, or in a lock briefcase when not in use

a. Please provide justification for use of hard copies
Hard copies of consent and assent are required and are kept as per institutional policy.

b. Will hard copies will be transported from one site to another, on or off campus?
No

B. Will any of the following subject identifiers be recorded (at any time) in association with the research data?
Yes

1) Indicate the subject identifiers that will be recorded. Check all that apply.
♦ Name
♦ DATES (e.g. date of study visit, date of sample collection, birth, admission, discharge)
Postal address information: street address, city, county, precinct, ZIP code
Telephone numbers
Fax numbers
Electronic mail addresses
Social Security numbers
♦ Medical Record numbers
Health plan beneficiary numbers
Account numbers
Certificate/license numbers
Vehicle identifiers and serial numbers, including license plate numbers
Device identifiers and serial numbers
Web Universal Resource Locators (URLs) Internet Protocol (IP) address numbers
Biometric identifiers, including finger and voice print
Full face photographic images [and any comparable images]
No Identifier

2) Will a unique subject identifying number (e.g., S1, S2, S3), characteristic or code be used to link data to any of the identifiers listed above?
Yes

a. Where will the key (that links the unique subject identification code to the subject's name or other identifier) be stored?
The link to the identifiers will be stored on the same secure server that the data is stored

b. Does the code number include the subject's initials or other subject identifier as part of the code?
No

3) What is the justification for recording the specific subject identifiers listed above? Check all that apply.
Schedule appointments
♦ Collect continuous clinical information from the medical records
♦ Follow-up with subjects
Link stored tissue with subject identification for it to be withdrawn in the future if requested
Compensation
Other. Explain.

4) How long will the subject identifiers be maintained in association with the research data?
This will be maintained for a period of at least 7 years following the completion of the study

5) How will all of the identifiable research data be destroyed (e.g., all identifiers stripped from the data and destroyed, hard copies shredded etc) when the identifiable data is no longer required?
All subject identifiers will be stripped from the database and destroyed per CH&MC/UNMC destruction policy, and any hard copies such as consent and assent forms will be shredded when the identifiable data is no longer required.

C. Will research data that contain subject identifiers be disclosed to:
Other investigators at UNMC, NM, UNO or CHMC who are not listed in Section I of this application?
No

2. Investigators outside of UNMC, NM, UNO or CHMC?
No

3. Will research data that contain subject identifiers be disclosed to any commercial sponsor or contract research organization (CRO), or to any other external organization or entity (e.g., NCI cooperative groups)?
No

D. What provisions will be in place to protect the subject's privacy? Check all that apply.
♦ Ensuring that only personnel listed on the IRB application Section I.3(A-E) are present during the consent process.
♦ Ensuring that the fewest number of individuals possible are aware of the subject's participation in the research.
♦ Ensuring that the research activities are performed in as private of a place as possible.
Other. Explain.

E. Does this research involve data banking at UNMC, NM, UNO or CHMC, or by an outside organization (e.g. NCI Cooperative Group, pharmaceutical company) for future research that is not related to this study?
No

RISK/BENEFIT ASSESSMENT

16. Potential Risks

What are the potential risks associated with each research procedure, intervention, evaluation and/or test? If data are available, estimate the probability that a given harm may occur and its potential reversibility.

There may be risk of abdominal distension and discomfort with air or carbon dioxide use and the risk of excessive CO2 absorption also exists.

The only study in pediatrics supporting possible CO_2 absorption when being used as an insufflation agent during upper endoscopy is the study that I carried out during my fellowship. In that study, 34% of non-intubated patients undergoing upper endoscopy with CO_2 insufflation experienced an elevation in end tidal CO2 level >/ 60 mmHg at some point during the procedure compared to only 4% in the air group. The manuscript for this study is in preparation. Other pediatric and adult studies do not show any safety concerns with CO_2 gas insufflation during upper endoscopy.

17. Risk Classification

What is the overall risk classification of the research?

Minimal risk

♦ Greater than minimal risk

18. Minimization of Risk

A. Describe how the subjects of the research will be monitored by the investigators and other research personnel to ensure their safety.

Previous studies in adults have documented safety and efficacy of CO_2 for insufflation in decreasing abdominal distension and discomfort. Patients will be continuously monitored throughout the procedure. If there is any evidence of respiratory distress or other potential CO_2 complications, the endoscopist will be unblinded; and CO_2 will be turned off if it is being used. Physicians will be immediately available throughout the procedure and prior to discharge from the procedure suite. They will also be available by phone 24/7/365.

B. Describe how the data collected will be monitored to ensure the safety of subjects. Identify who will perform the ongoing data and safety analysis, and describe the frequency of data analysis. If there is an independent Data and Safety Monitoring Board (DSMB) provide the charter, or describe (1) the composition of the DSMB membership, (2) the frequency of DSMB meetings and reports.

An interim safety analysis will occur after enrollment of the first half of the subjects are enrolled; 50 subjects in the GA group and 50 subjects in the MAC group. The principal investigator and co-investigators will take part in this analysis.

C. Describe the auditing plan for research conducted. Identify who will conduct the

audits and specify the audit frequency.
The principal investigator will conduct auditing of the data after every 50 subjects enrolled in the study.

D. Describe the specific subject withdrawal criteria.
If any potential risks is observed during the procedure such as with evidence of respiratory distress or other potential CO_2 complications, the endoscopist will be unblinded; and CO_2 will be turned off if it is being used and the subject will be withdrawn from the study.

E. Describe the stopping rules for the research (e.g., the specific criteria for halting or early termination of the study).
The research will be terminated early if there are significant reports of adverse events reported in an arm of the study. It will also be stopped early if significant results are reported during the interim analysis after enrollment of the first half of the subjects are enrolled. .

F. Describe plans and resources available to promptly address any subject injury.
Physicians will be immediately available throughout the procedure and prior to discharge from the procedure suite. They will also be available by phone 24/7/365.

19. Potential Benefits to the Subject
Is there the prospect for direct benefit (eg, research on diagnosis or treatment of disease)?
Yes

Describe potential benefits to the subjects that may reasonably be expected from participation in the research, if any. If there are therapeutic and non-therapeutic components of the research, address anticipated benefits to subjects that may reasonably be expected from each of these components.
Patients randomized to the CO_2 arm may benefit from less procedure pain when used during colonoscopy as a few pediatric studies have shown these benefits with the use of CO_2 for colonoscopy.

20. Potential Benefits to Society
Describe the potential benefits to society that may reasonably be expected to result from this research.
Publishing this work may encourage the use of safe and best insufflation practices in all children. If elevated end tidal CO_2 levels persist despite protection of the airway, then CO_2 use in children may be limited or restricted to only colonoscopy.

ALTERNATIVES TO PARTICIPATION

21. Alternatives to Participation

1. Describe the likely care the subject would receive at this institution were he/she not to participate in the research. If there are more than one reasonable courses of treatment briefly describe.

There is currently no standard of care at this institution regarding use of "CO_2" versus "air "as the insufflation gas. The gas of choice to be used is usually at the discretion of the endoscopist and the availability of carbon dioxide gas in the procedure room or OR.

2. Is the potential benefit of the research at least as good as the potential benefits of the alternatives described above?

Yes

3. Are there any reasonably available alternatives outside this institution which would have the potential for providing benefit to the subjects outside the research context?

No

4. Would any of the study procedures or courses of treatment in the protocol be available to the subject if they elected not to participate?

Yes

a. Explain.

If the subject refuses to participate in the study and requests carbon dioxide gas use for endoscopic insufflation based on the varst adult studies and limited pediatric studies; if carbon dioxide gas is available and the endoscopist wishes to use it despite its limited data on safety in children; it could be potentially offered to a subject who refuses to participate in the study as there is no standard of care at CHMC for insufflation gas. On the other hand, air is most readily available and if a subject requests air used for endoscopic insufflation, this could be used. However, subject may not benefit from the potential benefits of decreased post procedure pain associated with CO2 use reported in the few pediatric studies that compared CO2 use to air in colonoscopy.

5. Would the research intervention be available outside the context of research?

No

6. Are there any treatments that the subject would be denied as a consequence of participating in research that he/she would have received had he/she not participated?

No

7. How do the risks of the research compare with the risks of alternative procedures or courses of treatment described above?
The alternative gas for endoscopic insufflation is air. Even though, air may be associated with increased post procedure pain especially with its use in colonoscopy; there is no increased risk of excessive inhalation or systemic absorption of carbon dioxide with the use of air for insufflation.

FINANCIAL OBLIGATIONS AND COMPENSATION

22. Financial Obligations of the Subject
A. Who will pay for research procedures, interventions, evaluations and tests? Check all that apply.
Sponsor
Grant
CRC, CCTR
Costs or fees waived by Nebraska Medicine, UNMC- P, CHMC or CSP
Department/Section funds
♦ Other. Explain Although this study is supported by the UNMC Diversity and Inclusion grant; procedures and interventions are considered standard therapy and would be carried out regardless of research participation

B. Will any of these procedures, interventions, evaluations and tests will be charged to the Subject, the Subject's health insurance, or Medicare/Medicaid?
No

C. Are there any other financial obligations that the subject will incur as a result of participating in the study?
No

23. Compensation to the Subject for Participation
A. Will the subject receive any compensation for participation?
No

PRIOR REVIEW

24. Prior IRB Review
A. Has this study (or one substantially similar) been previously submitted to the UNMC IRB (or the Joint Pediatric IRB) and then withdrawn by the investigator for any reason?
No

B. To the best of your knowledge, has this study (or one substantially similar) been considered by another IRB and disapproved?
No

SUBJECT IDENTIFICATION & RECRUITMENT

25. Method of Subject Identification and Recruitment
A. Will prospective subjects be identified through initial contact by the investigator?
Yes

1. Identified through: Check all that apply.
♦ Clinic
♦ Hospital inpatient units
Previous research participants
♦ Investigator or clinic databases or registries
Hospital Opt-In Database (thru Nebraska Medicine, BMC or CHMC Conditions of Treatment)
School records
Support groups, or other Interest Groups
Other. Explain.

2. Describe how the research staff has ethical access to the potential subjects?
Research staff will have contact and ethical access to potential subjects. Subjects to be approached for enrollment have been evaluated by a pediatric gastroenterologist here at CHMC and scheduled for a procedure. Our research coordinators have access to patients scheduled for procedures when we identify the potential subject and give them their names.

3. Who will initially screen potential subjects to determine eligibility?
♦ Investigator with an existing clinical relationship
♦ Investigator with other legitimate access
Investigator whose professional responsibilities that require access to names of potential subjects
Honest broker (thru Nebraska Medicine or Bellevue Medical Center COT Opt-in database)
Research coordinator or other person without ethical access

B. Will prospective subjects make the initial contact with the research personnel to inquire about the study?
Yes

1. Potential Subjects learn about the research through: Check all that apply.
♦ Referral by clinician or other parties specifically for the research
Printed advertisements (including bulletins, newsletters, posters, fliers, and magazine or newspaper ads)
Radio and Television advertisements
Electronic advertisements (including social media or other on-line venue)
♦ Word of mouth
Public UNMC study database
♦ Other. Explain. When the Gastroenterology schedulers are calling families to schedule EGD/Colonoscpy procedures they will ask if it is okay to have research staff approach them about a study. If they say yes, the schedulers will make a note in their medical records and this will prompt the research coordinator to review their chart for inclusion/exclusion criteria. If the patient qualifies for the study, they will be approached the day of their visit regarding the study.

C. Will this study be listed in the clinical trial registry at www.clinicaltrials.gov?
Yes

1. Provide the NCT#.
NCT04541667

2. Identify who holds the NCT#
♦ PI
Sponsor

OBTAINMENT OF INFORMED CONSENT

26. Waiver or Alteration of Informed Consent
A. Is a complete waiver or alteration of consent requested?
No

27. Waiver of Signed Consent
Is a waiver to obtain signed consent requested?
No

28. Child Assent
A. Is a waiver of child assent requested?
No

29. Process of Informed Consent

A. When will the prospective subject/parent(s)/guardian(s)/LAR be approached relative to their/the subject's actual participation in the study?

Prospective subjects parents or legal guardians will be informed of the study at the time the subject is seen in the clinic or in the inpatient setting or when the decision is being made to schedule an endoscopic procedure. This is usually days or weeks to months prior to the procedure or actual study date.

B. Where will informed consent be obtained, and how will the environment be conducive to discussion and thoughtful consideration?

Consent procedures will be performed in a private room, either in the exam room in the clinic or in the private inpatient room or a privater pre-procedure room . Parents and legal guardians will be given the time to fully understand the study before the consent is obtained. It is possible that we will let the families know our GI research coordinator will be following up with them and give the names of the potential subjects to our research coordinator and they will follow-up with the family and e-mail them the consent form so the family can review the consent form in private at home. The research study coordinator would then follow-up with the family to see if they would like to participate in the study or not.

C. Who will be involved in the process of consent and what are their responsibilities?

The principal investigator, some of the co-investigators (A.H. D.F.) and study coordinators will be involved in the consenting process. The other responsible personnel may inform the patients about the study but will not be involved in the consenting process.

D. How much time will be allotted to the process of consent?

When possible, we will discuss the study and obtain consent in the clinic prior to the day of the procedure or in the inpatient setting. Otherwise, consent will be obtained before the procedure; family members present will be included in the discussion. Duration of the consenting process will vary from one family to the other depending on how long it takes to answer all their questions. As much time that is needed will be allowed for the consenting discussion and process.

E. How will the process of consent be structured for subjects who are likely to be more vulnerable to coercion or undue influence?

All patients will have been seen by a member of our clinical team (Pediatric Gastroenterology) in the clinic prior to the procedure or in the inpatient setting. Patients who need a diagnostic or therapeutic endoscopy will be scheduled for the procedure. The need for an endoscopic procedure will identify them to the research team as a candidate. In some cases, the enrollment will happen in the clinic at the time the need for endoscopy is

identified, particularly when a research team member is seeing the patient. In other cases, potential subjects will be identified by review of scheduled procedures on the day of the procedure. Subjects who have not been offered participation in the study in the clinic will then be approached in the procedure unit on the day of the procedure by a member of the research team.
During enrollment, we will emphasize that we will provide the same quality of care regardless of their participation, and that no stigma will be attached to them if they prefer not to give consent.
We will involve all family members present during the consent process and will explain the consent form in detail.
Prior to signing the consent, we will ask if they have any questions and if they have fully understood the study.
We will discuss their options such as not participating if they choose.
We will also assess if a subject advocate is needed and should one be needed then one will be appointed.

F. Will non-English speaking subjects be enrolled in this research?
Yes

Describe the plan to conduct the process of informed consent in the language of the subject/parent(s)/guardian(s)/LAR
We have developed Spanish consents for this study. All of the subjects are appointed an interpreter if Spanish speaking that the CARES RN works with to see the patient. The Interpreter will also be utilized to approach the family and subject for this study. Dr. Huang is fully fluent in Spanish so he will not use an interpreter. The study coordinator will ensure an interpreter is utilized when Dr. Huang is not available.

G. How will it be determined that the subject/parent(s)/guardian(s)/LAR understood the information presented?
At the end of the consenting process, subjects, parents and legal guardians will be asked a series of questions at the appropriate grade level to ensure they full understand the study. We will also ask them if they have any questions. The consent form will be only signed when they have fully understood the study and voluntarily wish to participate in the study.

30. Documentation of Informed Consent and Assent
Select who will obtain consent from the subject/parent(s)/LAR.
Choudhry, Ojasvini C

Dike, Chinenye Rebecca

Freestone, David J

Huang Pacheco, Andrew Steve S

Kusek, Mark E

Quiros, Ruben E

Shukry, Mohanad

31. Consent Forms and Study Information Sheets
Indicate the type of consent forms and study information sheets to be used in this research. Check all that apply.
Adult consent form
Legally authorized representative (LAR) consent form
♦ Parental/Guardian consent form
♦ Youth study information sheet
♦ Child study information sheet
Adult study information sheet (decisionally-impaired)
Screening consent form
Addendum consent form
♦ Other. Explain. Spanish Child Information Sheet and Spanish Parental/Adult ICF

32. Information Purposely Withheld
Will any information be purposely withheld from the subject during the research or after completion of the research?
Yes

A. What specific information will be withheld?
The arm of randomization "air" versus "CO_2" gas use for insufflation willl be purposely withheld from the subjects and their family.

B. What is the justification for this non-disclosure?
To avoid all forms of bias; patients, endoscopists and anesthesiologists will be blinded to the arm of randomization; gas used for endoscopic insufflation

C. Will information that has been withheld eventually be shared with the subject?
No

1. Provide justification.
To protect the integrity of the research and the results; blinding will continue until statistical analysis has been done before the arm of randomization will be unmasked. Individual patients will not be informed. However, the results of the research will be presented in scientific meetings and published. The results of this research will help guide our practice on the safety of CO_2use for insufflation during upper endoscopic related procedures in children.

RESOURCES

33. Describe the resources available to safely conduct this study at <u>each</u> study sites specified in Section I.7.
The availability of physicians (anesthesiologists and pediatric gastroenterologists) at CHMC and most of the pediatric GI procedures are performed at CHMC makes it the ideal site to safely and successfully conduct this study

LITERATURE REVIEW

34. References
Provide a full listing of the key references cited in the background (Section II.3). The references should clearly support the stated purpose of the study.
1 Steppan J, Hogue CW, Jr. Cerebral and tissue oximetry. Best Pract Res Clin Anaesthesiol 2014;28(4):429-39.
2 Lo SK, Fujii-Lau LL, Enestvedt BK, et al. The use of carbon dioxide in gastrointestinal endoscopy. Gastrointest Endosc 2016;83(5):857-65.
3 Chen SW, Hui CK, Chang JJ, et al. Carbon dioxide insufflation during colonoscopy can significantly decrease post-interventional abdominal discomfort in deeply sedated patients: A prospective, randomized, double-blinded, controlled trial. J Gastroenterol Hepatol 2016;31(4):808-13.
4 Liu X, Liu D, Li J, et al. [Safety and efficacy of carbon dioxide insufflation during colonoscopy]. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2009;34(8):825-9.
5 Lynch I, Hayes A, Buffum MD, et al. Insufflation using carbon dioxide versus room air during colonoscopy: comparison of patient comfort, recovery time, and nursing resources. Gastroenterol Nurs 2015;38(3):211-7.
6 Memon MA, Memon B, Yunus RM, et al. Carbon Dioxide Versus Air Insufflation for Elective Colonoscopy: A Meta-Analysis and Systematic Review of Randomized Controlled Trials. Surg Laparosc Endosc Percutan Tech 2016;26(2):102-16.
7 Riss S, Akan B, Mikola B, et al. CO2 insufflation during colonoscopy decreases post-interventional pain in deeply sedated patients: a randomized controlled trial. Wien Klin Wochenschr 2009;121(13-14):464-8.
8 Sajid MS, Caswell J, Bhatti MI, et al. Carbon dioxide insufflation vs conventional air

insufflation for colonoscopy: a systematic review and meta-analysis of published randomized controlled trials. Colorectal Dis 2015;17(2):111-23.
9 Singh R, Neo EN, Nordeen N, et al. Carbon dioxide insufflation during colonoscopy in deeply sedated patients. World J Gastroenterol 2012;18(25):3250-3.
10 Homan M, Mahkovic D, Orel R, et al. Randomized, double-blind trial of CO2 versus air insufflation in children undergoing colonoscopy. Gastrointest Endosc 2016;83(5):993-7.
11 Kresz A, Mayer B, Zernickel M, et al. Carbon dioxide versus room air for colonoscopy in deeply sedated pediatric patients: a randomized controlled trial. Endosc Int Open 2019;7(2):E290-e97.
12 Thornhill C, Navarro F, Alabd Alrazzak B, et al. Insufflation With Carbon Dioxide During Pediatric Colonoscopy for Control of Postprocedure Pain. J Clin Gastroenterol 2017.
13 Eastwood GM, Tanaka A, Bellomo R Cerebral oxygenation in mechanically ventilated early cardiac arrest survivors: The impact of hypercapnia. Resuscitation 2016;102(11-6.
14 Erdogan S, Oto A, Bosnak M Reliability of cerebral oximeter in non-invasive diagnosis and follow-up of hypercapnia. Turk J Pediatr 2016;58(4):389-94.

SECTION III

SUBMISSION DEADLINE

A. Full Board Review:
The IRB meets twice monthly, on the first and third Thursday of the month, with the exception of January and July when the IRB meets only on the third Thursday of the month. No more than 15 applications (e.g., initial review of a new study, re-review of a tabled study) will be reviewed at each meeting. All reviews are performed on a first-come first-served basis. The IRB meeting schedule and deadline dates can be found on the IRB website at www.unmc.edu/irb.

B. Expedited Review
Applications that qualify for expedited review have no submission deadline and can be reviewed independent of the IRB meeting schedule. Call the Office of Regulatory Affairs for assistance in determining if your study meets the requirements for expedited review.

ADDITIONAL REVIEW REQUIREMENTS

Final IRB approval and release of studies is contingent upon approval by the following UNMC committees or departments. Check the appropriate boxes:
♦ **Conflict of Interest Committee (COIC):** All responsible personnel listed in Section I of the IRB application (e.g., PI, Secondary Investigator, Participating Personnel, and Coordinator(s)) must disclose **any** financial interest in the research. Data and Administrative Personnel are exempt. The COIC will review any financial interest which is classified as significant.
Institutional Biosafety Committee (IBC): Review by the IBC is required for all protocols involving the use of gene transfer and vaccines.
Pharmacy and Therapeutics (P&T) Committee: Review by the P&T Committee is required for all protocols involving the use of investigational or marketed drugs.
Radioactive Drug Research Committee (RDRC): Review by the RDRC is required for all protocols involving the use of a radio-labeled drug for which the investigator or the institution holds the IND.
Sponsored Programs Administration (SPA)/Office of Regulatory Affairs: For commercial sponsored studies, the consent form and contract will be compared for consistency by the ORA. Final IRB approval and release is contingent upon completion of a signed contract, verified by SPA, for all commercially sponsored research.
UNMC Eppley Cancer Center Scientific Review Committee (SRC): Review by the SRC is required for all protocols involving cancer patients.

Other Review
No Additional Reviews Required