

HUMAN SUBJECT RESEARCH PROTOCOL-FORM I

NOTE: For the purpose of this Form, Mass. Eye and Ear (MEE) include the Massachusetts Eye and Ear Infirmary (MEEI), and Schepens Eye Research Institute, Inc. (SERI). MEEI is a HIPAA-covered entity; SERI is not considered a covered entity.

DATE: 10/06/14

TITLE OF PROJECT: Prophylactic antibiotics after functional endoscopic sinus surgery: a randomized, double-blind placebo controlled trial

PRINCIPAL INVESTIGATOR: Eric Holbrook

FUNDING SOURCE: Dr. Holbrook / Dr. Gray

1) Does your research involve the following? Check all that apply:

- Use of investigational drugs or biologics
- Use of investigational devices
- Use of human embryonic stem cells
- Use of rDNA, microbiological agents, gene transfer, transplantation of animal tissues

2) Is this study a Clinical Trial? YES NO

IF YES, submission of an industry-sponsored protocol or SUPP M is required. If no, SUPP N should be submitted.

2b) Who will register the study with clinicaltrials.gov?

This is a Phase I or a pilot study-registration is not required Sponsor PI
other: Already registered - NCT01919411

3) Provide a brief summary of the proposed research (in language that can be understood by a non-scientist):

RESPONSE: Functional endoscopic sinus surgery (FESS) is a commonly performed procedure in the United States to treat chronic rhinosinusitis. Common practice is to prescribe prophylactic antibiotics postoperatively. This is similar to the long tradition of prophylactic antibiotics after tonsillectomy. The American Academy of Otolaryngology - Head and Neck Surgery recently strongly recommended against prophylactic antibiotics after tonsillectomy. In this light, this study would demonstrate the lack of need for antibiotics after FESS. Currently Dr. Holbrook does not prescribe antibiotics except when evidence of active infection was found during surgery. Dr. Gray currently prescribes antibiotics. This study would prospectively compare the two groups in a randomized fashion. Two previous studies have been performed (Jiang et al. Postoperative antibiotic care after functional endoscopic sinus surgery. *Am J Rhinol* 22, 608-612, 2008); (Albu, et al. Prophylactic antibiotics in endoscopic sinus surgery: A short follow-up study. *Am J Rhinol* 24 306-309, 2010.) These studies were both randomized, placebo controlled prospective studies. Albu et al found that amoxicillin/clavulanate improved the outcome in the "early blood crust healing" and the endoscopic score was improved. Jiang et al. showed that amoxicillin/clavulanate did not improve short term outcomes of FESS. Both studies were limited by a lack

of a prospective instrument to evaluate symptoms. We plan to use the Sinonasal outcomes test -22 (SNOT-22), which is a validated quality of life instrument in sinusitis.

4) What is the estimated completion date? (MM/YYYY)

RESPONSE: 06/2015

5) Who specifically (name, title, and department) is going to perform the coordinator function? Discuss his/her relevant qualifications (training, education, experience):

The PI, Dr. Holbrook, has assumed coordinator function. He has had experience and training through the Harvard Catalyst education offerings in clinical studies.

6a) Who is going to supervise the study coordinator(s)? When applicable, indicate if support and oversight will be provided by the Ophthalmology Clinical Research Office (OCRO).

6b) Describe the PI's plan to provide adequate training, and supervision (e.g., regular meetings, training opportunities):

Dr. Holbrook will be supervising all aspects of the study and meets regularly (weekly) with Dr. Gray on matters of enrollment, patient compliance, and monitoring of adverse events.

7) Delegation of Significant Study-Related Tasks- If non-physicians are tasked to assess clinical response to an investigational therapy, provide medical care to subjects during the course of the study, assess inclusion/exclusion criteria, and evaluate adverse events, list their names in the table below and complete:

Name	Delegated Tasks	Qualifications- Licensing, or Certification	Training
Dr. Holbrook / Dr. Gray	Enrollment, follow-up, evaluation for adverse reactions, data collection	MD	Residency and fellowship training in otolaryngology and rhinology
Pharmacy staff (supervised by Dr. Christine Finn)	Distribution of study drug	Pharm D	Doctorate in pharmacy

8) Indicate all MEE sites where research activities occur:

- Boston-MEEI 243 Charles Street
- Boston Longwood Medical Area – 800 Huntington Ave
- Boston-SERI 20 Staniford St.
- Braintree - 250 Pond St
- Concord - 54 Baker Ave Ext
- Duxbury - 20 Tremont St, Route 3A
- East Bridgewater - 400 N. Bedford St

- Milton - 100 Highland St.
- Newton - 2000 Washington St
- Quincy - 500 Congress St, Crown Colony Office Park
- Stoneham - One Montvale Ave
- Stoneham - Retina Consultants-3 Woodland Rd
- Weymouth - 825 Main St

9) Are there any non-MEE sites involved in this study? YES NO (If NO, skip to question 11)

IF YES, Is MEE the lead site or coordinating center? YES NO

10) In the table below, list each non-MEE sites where research activities will occur, and the status of IRB review at each site (indicate if the intent is for MEE to serve as the IRB of record for all study sites (cede review) or if IRB review will be required at other sites:

Non-MEE Sites	IRB Review Status (i.e., review pending, approved, seeking cede review)

SUBJECT INFORMATION

11) In the table below, please indicate age range, gender, total number of subjects to be enrolled at MEE, and if multi-site, total number for the study:

	Age Range	Total Number at MEE	Total Number for the Study (if multi-site)
Adults (over 18)	18- no limit	140	140
Children (under 18)	NA	0	

12) Is a gender being excluded from this study? YES NO

IF YES, provide scientific justification:

Response:

13) Select all populations that may/will be enrolled (will not be excluded from the study) below. For some populations you may be asked to provide additional information.

- Pregnant Women
- Employees/Staff of MEEI or SERI-please specify:
- Healthy Controls

- Students/ Residents/ Fellows or other trainees
- Children
- Prisoner
- Non-English Speaking Subjects
- Adults with Decisional Impairment- If checked, please describe below the type and range of decisional impairment and a rationale for why it is necessary to include adults with decisional impairment:
- Other Populations with Potentially Diminished Capacity (i.e., socially, educationally, economically disadvantaged, elderly, terminally ill) - If checked, specify population below and describe what additional safeguards will be in place to protect the rights and welfare of these subjects:

RESPONSE: We have enrolled approximately 25 patients so far. We would prefer to enroll non-english speaking patients. We are aware of the new IRB protocol regarding non English speaking patients' consent. We would like to apply for the "short-form" consent process in order to continue to enroll non-English speaking patients.

- 14)** Explain how the Investigator has access to a population that would allow recruitment of the required number of subjects within the proposed timeframe:

RESPONSE: Dr. Holbrook and Dr. Gray both have busy rhinology practices from which to enroll patients.

- 15)** If subjects are recruited from the investigator's patient population or MEE/SERI employees will be recruited, describe what measures are taken to minimize coercion or undue influence:

RESPONSE: The investigators discuss with the patient the voluntary nature of the study, and the fact that the subjects can withdraw at any time from the study. Also it is discussed with the patient that by not enrolling they will not affect their clinical care at all.

SUBJECT SCREENING/RECRUITMENT

- 16)** Describe any screening methods used to determine eligible subjects (i.e., search of medical records or recruitment databases, completion of screening tests, response to interview questions, etc.):

RESPONSE: Patients will be recruited by Dr. Gray and Dr. Holbrook in their clinics from patients that are determined to be candidates for endoscopic sinus surgery and have agreed to undergo surgery. The patient will decide to undergo surgery first, and will then be asked to participate in the study. A script to be used for oral invitation in the study is provided in the application packet.

- 17)** Is [protected health information](#) accessed during the screening process? **YES** **NO**

IF YES, specify the information system(s) and the location of the database(s) you will be accessing during the screening process:

RESPONSE: LMR is accessed for patients' clinical information. This is accessed in the MEEI sinus center.

18) Is [protected health information](#) recorded during the pre-screening process? YES NO

IF YES, list the identifiers that are recorded prior to obtaining consent:

RESPONSE:

19) Describe the recruitment process (the process by which potential subjects are informed about the availability of the research), who is responsible for recruitment, and how (i.e., use of flyers, advertisements, letters, and oral scripts, etc.) and when subjects will be recruited:

RESPONSE: Patients will be recruited by Dr. Gray and Dr. Holbrook in their clinics from patients that are determined to be candidates for endoscopic sinus surgery and have agreed to undergo surgery. The patient will decide to undergo surgery first, and will then be asked to participate in the study. A script to be used for oral invitation in the study is provided in the application packet.

20) Does the recruitment strategy involve contacting individuals multiple times? YES NO

IF YES, describe the frequency and in what manner individuals will be contacted:

RESPONSE:

21) Are you using email to recruit subjects? YES NO

IF YES, describe the use of email and include a copy of the email text below:

RESPONSE:

22) Will fliers, letters and/or brochures be posted, mailed or otherwise distributed? YES NO

IF YES, please describe how each document will be used:

RESPONSE:

NOTE: HIPAA does not permit non-MEE physicians to disclose patient information to Mass. Eye and Ear for research recruitment purposes other than for treatment purposes or pursuant to a HIPAA authorization. Non-MEE physicians may inform their patients of a research study and allow the patients to self-disclose their interest to the study team.

23) Describe whether physician referral is used and whether subjects healthcare providers be notified of their patients' participation in the study?

RESPONSE: Dr. Gray and Holbrook are rhinology specialists. They are referred patients from community otolaryngologists for management of chronic sinusitis. This involves medical as well as surgical management. Referring otolaryngologists would not be notified of patient participation.

COMPENSATION/COSTS

- 24) Will subjects be paid/offered a recruitment incentive or reimbursed for participating in the research?
 YES NO

IF YES, please describe the amount and type of payment or reimbursement (e.g. parking vouchers) and the proposed method and timing of disbursement and why this is reasonable and non-coercive:

RESPONSE:

- 25) Will there be any out-of-pocket costs to subjects and/or expenses likely to be covered by their insurance for participating in the study? YES NO

IF YES, please specify in detail the costs to subjects and/or their insurance (e.g. co-pays):

RESPONSE: The study drug is provided by the pharmacy free of charge. The study medication supplies are charged to the study's cost center by the pharmacy.

- 26) If applicable, how will the cost of reasonably foreseeable medical care in the event of a research-related injury be covered (e.g., sponsor agreement, likely to be covered by insurance, grant, departmental funds)?

RESPONSE: This would be covered by patients' insurance.

RISK

Risk is the probability and magnitude of harm or discomfort anticipated as a result of participation in the research. Any risks of harm to subjects and/or anticipated discomfort(s) that are reasonably foreseeable, even if unlikely, and the safeguards in place to minimize these risks and discomfort(s) must be identified and discussed below. Risks of harm and discomfort may include: physical harm/discomfort, psychological harm/discomfort, legal harm/discomfort, social harm/discomfort, and economic harm.

- 27) Describe any risks of harm to subjects that are reasonably foreseeable, even if unlikely:

These are listed below:

1. amoxicillin/clavulanate arm:
From the FDA monograph
Gastrointestinal

Diarrhea, nausea, vomiting, indigestion, gastritis, stomatitis, glossitis, black “hairy” tongue, mucocutaneous candidiasis, enterocolitis, and hemorrhagic/pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment

Hypersensitivity Reactions

Skin rashes, pruritus, urticaria, angioedema, serum sickness–like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, myalgia, and frequently fever), erythema multiforme (rarely Stevens-Johnson syndrome), acute generalized exanthematous pustulosis, and an occasional case of exfoliative dermatitis (including toxic epidermal necrolysis) have been reported. These reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Whenever such reactions occur, the drug should be discontinued, unless the opinion of the physician dictates otherwise. Serious and occasional fatal hypersensitivity (anaphylactic) reactions can occur with oral penicillin.

Liver

A moderate rise in AST (SGOT) and/or ALT (SGPT) has been noted in patients treated with ampicillin-class antibiotics but the significance of these findings is unknown. Hepatic dysfunction, including increases in serum transaminases (AST and/or ALT), serum bilirubin, and/or alkaline phosphatase, has been infrequently reported with Augmentin. It has been reported more commonly in the elderly, in males, or in patients on prolonged treatment. The histologic findings on liver biopsy have consisted of predominantly cholestatic, hepatocellular, or mixed cholestatic-hepatocellular changes. The onset of signs/symptoms of hepatic dysfunction may occur during or several weeks after therapy has been discontinued. The hepatic dysfunction, which may be severe, is usually reversible. On rare occasions, deaths have been reported (less than 1 death reported per estimated 4 million prescriptions worldwide). These have generally been cases associated with serious underlying diseases or concomitant medications.

Renal

Interstitial nephritis and hematuria have been reported rarely. Crystalluria has also been reported

Hemic and Lymphatic Systems

Anemia, including hemolytic anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, and agranulocytosis have been reported during therapy with penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. A slight thrombocytosis was noted in less than 1% of the patients treated with Augmentin. There have been reports of increased prothrombin time in patients receiving Augmentin and anticoagulant therapy concomitantly.

Central Nervous System

Agitation, anxiety, behavioral changes, confusion, convulsions, dizziness, insomnia, and reversible hyperactivity have been reported rarely.

Miscellaneous

Tooth discoloration (brown, yellow, or gray staining) has been rarely reported. Most reports occurred in pediatric patients. Discoloration was reduced or eliminated with brushing or dental cleaning in most cases.

2. Placebo Arm:

The main theoretical risk from not giving antibiotics post operatively would be a risk of postoperative infection. This would manifest as sinusitis-like symptoms. Worst case scenario would result in complications of sinusitis (orbital infection, meningitis, brain abscess). These complications are rare, and Dr. Holbrook has not experienced them while not giving routine postoperative antibiotics as is his usual practice.

3. Privacy:

Personal data will be collected from subjects. The data will be saved under a unique subject number, which will remove personal identifying information from the research data. Data will be secured under a password protected computer in a locked office of the PI.

28) If applicable, describe any group harms (i.e., research that focuses on a specific group or population):

RESPONSE: NA

29) Do you anticipate any circumstances in which a “breach of confidence” associated with a mandated disclosure (e.g. reporting abuse to authorities) may occur as part of this study?

RESPONSE: No we do not anticipate a breach of confidence

30) In the view of the PI, what risk classification (taking into consideration the probability and magnitude of harm) is appropriate for the proposed research?

Minimal Risk Greater than Minimal Risk Unknown

Minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

31) Please explain why you feel this category is appropriate based on the definition above (when more than minimal risk describe the likelihood and seriousness of such risks):

RESPONSE: In patients that are randomized to receive post operative antibiotics, there is a risk of adverse reaction to augmentin as detailed above. For patients that are randomized to placebo, there is a risk of post operative infection as detailed above as well. We believe the study is low risk to participants, however as defined above, it is more than the risk encountered in daily life.

32) What provisions are in place to minimize harm or discomfort?

RESPONSE: Patients are seen one week after surgery to undergo endoscopic evaluation to ensure that the patient is healing well without evidence of infection. At all times during the day they can call the sinus center to speak to a nurse if they have any concerns. At night there is a resident on call to answer questions and the MEEI ED is always open.

ALTERNATIVES

33) Describe any alternatives, especially other treatment(s) that are available to potential patients outside of the research:

RESPONSE: If patients do not elect to enroll in the study, they would receive standard post-operative care. They would be prescribed antibiotics at the discretion of the surgeon.

BENEFITS

- 34) Are there any potential direct benefits to individual subjects related to the research?
 YES NO

IF YES, please explain (address whether these benefits (e.g., clinical, therapeutic) would be available to subjects outside of the research):

RESPONSE:

- 35) Explain the potential benefits to science, and/or society (indirect benefits) which may accrue as a result of this research:

RESPONSE: Antibiotic resistance is growing in the world, and this study may provide prospective, randomized data that antibiotics do not result in a benefit to patients. Hopefully surgeons would stop giving postoperative antibiotics, and decrease the risk of side-effects from antibiotics (allergic reactions, clostridium difficile infection, GI upset, etc) to future patients. Also health care costs would be decreased by reducing antibiotic prescriptions.

- 36) If more than minimal risk, address how risks relate to benefits:

RESPONSE: While not “minimal risk”, the risk to patients is low, as detailed above. Many patients have adverse reactions to antibiotics, and if this study shows that the outcomes of patients undergoing sinus surgery without antibiotics are not worse, then hopefully less patients will be prescribed antibiotics.

CONSENT PROCESS

- 37) Describe the consent process in detail. Include who specifically will be obtaining consent, describe their knowledge/experience in obtaining consent from research subjects, and include the location where study information will be exchanged, how (consent form, orally, information sheet, etc.) information is being conveyed to subjects, and when the consent will be obtained (e.g. during pre-surgical visit, about one week before the screening visit):

RESPONSE: Consent will be obtained by Dr. Gray, Dr. Meier or Dr. Holbrook in the clinic during the subject's preoperative visit in the MEEI sinus center. There is a formal consent form that is signed by patients and an oral script (these are on IRBNET). Subjects can think about the study and opt out of randomization at the time of surgery (usually 2-4 weeks elapse between preoperative visit and surgery).

- 38) Indicate which of the following consent procedures you are contemplating for this research:

Written consent form

- Short form process (only appropriate for minimal risk studies)
** If checked, answer question 42 below.*
- Assent from adults with diminished decision-making capacity
**If checked, provide justification below:*
- Assent from children and parental permission
- Oral consent or implied consent (e.g. completing a survey)
**If checked, provide justification based on [45 CFR 46.117\(c\)](#) below:*
- Requesting a waiver of informed consent from the HSC
**If checked, provide justification based on [45 CFR 46.116\(c\) and \(d\)](#) below:*

RESPONSE:

- 39)** Describe any foreseeable circumstances and/or reasons under which the subject's participation in the research may be terminated:

RESPONSE: If the patient does not want to participate further then they may opt out at any time during the study.

- 40)** How is subject comprehension assessed initially and throughout the consent process? Is the manner in which information is presented appropriate for the population? In cases where subject comprehension is severely limited what special provisions have been made (is there a third party involved in the consent process)? Discuss below:

RESPONSE: The investigators will describe the study according to the oral script and ask the patient if they understand everything that has been explained to them. We will ask them if they have any questions and answer them to their satisfaction. If the patients' comprehension is severely limited then we will not include them in the study.

- 41)** If the research-related intervention or interaction will occur on the same day that the subject initially receives information about the study, justify why this is appropriate/necessary:

RESPONSE: It will not be on the same day, patients will be enrolled at their post operative visit.

- 42)** Describe additional provisions in place for non-English speaking subjects (view [guidance](#)), including the availability/presence of translators (fluent in both English and the subject's spoken language) during the consent process and the translation of consent documents in a language understandable to them (when consent documents are translated all translated versions must be accompanied by an attestation from the translator) **OR** justify why non-English speaking subject are being excluded from the research:

RESPONSE: We would like to apply for use of the short form consent process for patients that do not speak English. We have used translators for patients that are not English speakers previously.

43) How will literacy be assessed? If subjects cannot read the consent form, describe the process for providing information to these subjects (i.e., reading the information aloud) and for documenting consent, including whether or not the short form (45 CFR 46.117(b) (2)) process will be utilized:

RESPONSE: This has not come up in the year of our trial. We would ask subjects if they understand the written consent form. If they are not literate, then we would use the oral script and document their understanding.

44) For Ophthalmology related studies, describe if the cohort is capable of reading the consent form and if not, describe exacerbating factors (visual impairment, eyes dilated at the onset of the study, etc.). In these cases, describe additional measures you will take to ensure comprehension of study-related information to promote informed decision-making by the subject:

RESPONSE: NA

45) For Otology related studies, describe if the cohort is capable of comfortably hearing the Investigator during the consent process and if not, describe exacerbating factors (hearing aid, cochlear implant, hearing impaired, etc.). In these cases, describe additional measures you will take to ensure comprehension of study-related information to promote informed decision-making by the subject:

RESPONSE: NA

INCIDENTAL FINDINGS

46) Is there a possibility of clinically significant incidental findings (information relating to previously undiagnosed medical or psychiatric conditions) being discovered during research procedures?

YES NO

IF YES, please outline the plan for addressing incidental findings (i.e., contacting the subject's primary care provider, referral etc.) including if and how subjects will be informed:

RESPONSE:

DISSEMINATION OF RESULTS

47) Describe any plans to share research results with subjects, this may include sharing individual results and/or aggregate results and may also serve as an opportunity to follow-up with subjects and **thank** them for participating in the research, particularly in cases where there is no direct benefit to the subject. If there are no plans to share results explain why this is not feasible, appropriate or applicable to this research:

RESPONSE: We would plan on disseminating the final publication paper to the subjects with a note of thanks when the research is completed.

48) How will results be published, and in what form (i.e., subjects will not be individually identifiable in publications):

RESPONSE: Results will be published in an otolaryngology peer-reviewed journal. There will be no identifiable information in the publication.

PRIVACY/CONFIDENTIALITY

Insofar as they apply, investigators are required to adhere to MEE Information Security Policies and Procedures. Therefore, research protocols must be designed in accordance with these requirements. On occasion the HSC may require additional provisions related to the use and security of research data. The HSC evaluates the collection and use of data based on the minimum necessary standard, the data necessary to satisfy the purposes of the research to carry out research-related activities. The HSC may require that when a research project collects personally identifiable, sensitive information that the PI obtain a Certificate of Confidentiality.

49) Describe the provisions in place to respect the privacy of subjects throughout the research:

RESPONSE: For each subject in the study, a unique identification number will be generated, this number will be used with their study responses and all results from the study. A list linking patients' names, MRN and unique ID will be created and stored on a password-protected computer only accessible by the PI. The survey responses with the unique identifiers will be locked in the PI's office. Only the PI will have access to this list. Pharmacy will have access only to the unique ID, and will be in charge of randomization.

50) Check all identifiers that will be obtained by investigators for the purposes of this study.

- | | |
|--|---|
| <input checked="" type="checkbox"/> Name | <input type="checkbox"/> Telephone Number |
| <input type="checkbox"/> Social Security Number | <input type="checkbox"/> Fax Number |
| <input checked="" type="checkbox"/> Medical Record Number | <input type="checkbox"/> Email Address |
| <input type="checkbox"/> Address by Street Location | <input type="checkbox"/> Web URLs |
| <input type="checkbox"/> Address by Town/City/Zip Code | <input type="checkbox"/> Internet Protocol (IP) Address |
| <input type="checkbox"/> Health Plan Beneficiary Number | <input type="checkbox"/> Account Number |
| <input type="checkbox"/> Certificate/License Number | <input type="checkbox"/> Ages over 89 |
| <input type="checkbox"/> Full Face Photographic Image | |
| <input checked="" type="checkbox"/> Elements of Dates except Year (Admission/Discharge Date, Procedure Date, Date of Birth or Death) | |
| <input type="checkbox"/> Vehicle ID Number and Serial Number Including License Plate Number | |
| <input type="checkbox"/> Medical Device Identifiers and Serial Number | |
| <input type="checkbox"/> Biometric Identifiers (e.g. finger or voice prints, retinal images) | |
| <input type="checkbox"/> None of the listed identifiers will be recorded as part of this study. | |
| <input type="checkbox"/> Other unique identifiers or code that can be used to identify the participant: | |

51) Investigators should only obtain the minimum data necessary to achieve research goals. Please justify why the data you are obtaining is the minimum necessary:

RESPONSE: We need the patients' names, date of birth, and MRN to identify patients. A unique number will be generated that will deidentify the patients to the pharmacy.

52) Will data about individual subjects be collected from sources outside of Mass. Eye and Ear?
 YES NO

IF YES, list each source (include if the source is considered a covered entity), the data collected, and any agreements in place to allow transfer of this data:

RESPONSE:

53) *Sensitive information* includes (but is not limited to) information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information that, if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples.

Will this research collect sensitive information? YES NO (If NO, skip to question 55)

IF YES, list the data that will be collected and provide a rationale under the *minimum necessary* standard:

RESPONSE:

54) Has a [Certificate of Confidentiality](#) been sought for this research? YES NO

IF YES, include a copy of the certificate at the time of submission or provide information related to the status of your application

IF NO, justify your response below:

55) Please indicate the specific safeguards in place to protect the confidentiality of subject data:

Administrative Safeguards:

YES NO Each member of the study team has completed Mass. Eye and Ear Privacy Training and Information Security Awareness Training and this training is up to date.

YES NO Paper files, electronic data, computing devices and storage media will be safeguarded in accordance with Mass. Eye and Ear Privacy and Information Security policies and procedures, including, but not limited to the safeguards more specifically identified below:

Physical Safeguards:

YES NO N/A Paper files will be locked in cabinets when not in use

YES NO N/A Paper files will be protected from inappropriate access when in use

- YES NO N/A Mobile computing devices and storage media will be locked in cabinets when not in use
- YES NO N/A Computing devices will be protected from inappropriate access when in use
- Yes No N/A Research data will be coded using a subject identification number that does not include the subject's initials and is not derived from the subject's identifiable information.

IF YES: The key linking the subject identification number to the subject's identifiable information is available only to the following study team members:

- Mass. Eye and Ear PI
- Other Mass. Eye and Ear study team members
- External investigator
- External sponsor

- Yes No The key will be stored separately and in a locked cabinet (if paper)
- Yes No The key will be stored separately and on a password protected network drive with access limited to those people identified above

Technical Safeguards:

- YES NO Electronic data will be stored on Mass. Eye and Ear network folders for which access is limited to authorized members of the study team only
- YES NO To the extent that electronic data is collected on the hard drive of a computing device, it will be promptly and securely transferred to a secure folder within the Mass. Eye and Ear network
- YES NO Mobile devices (including but not limited to laptops, tablet computers, smart phones, external hard drives and USB drives) containing electronic data will be encrypted
- YES NO Remote access to electronic data will be gained through Information Systems
- YES NO Electronic data will be encrypted when transmitted outside of Mass. Eye and Ear

Please describe any additional safeguards that will be used to protect the study data and explain any "No" responses:

RESPONSE: We will not use remote access, and we will not send data outside of MEEI.

- 56)** Will data that identifies individual subjects be disclosed to parties outside of Mass. Eye and Ear (e.g. sponsor and/or coordinating center, research registry) for purposes of the research? YES NO

IF YES, list the parties and explain how and what information will be shared:

RESPONSE:

57) Where will research data, including the signed informed consent form and assent be stored (e.g., MEEI medical record, research record, etc.).

RESPONSE: In the MEEI Sinus center under lock and key.

58) Please provide the plan for destroying identifiers (at the earliest opportunity as consistent with the research plan) or provide a health or research justification for retaining identifiers. For protocols subject to future and secondary data analysis, provide justification for not destroying identifiers permanently and explain plans for future use (i.e., establishment of a data or specimen repository):

RESPONSE: When the research is complete, we will destroy all identifiable information by following MEEI protocols.

CONFLICTS OF INTEREST

If the research involves any of the following: **1) for-profit sponsor or funding source; 2) a marketed drug, device, or other technology; or a drug, device, or other technology in development; or 3) a new technology, software, or therapeutic approach**, all investigators are required to complete and submit (at the time of initial submission and thereafter in accordance with the policy) a Conflict of Interest in Research: Project-Specific Disclosure (SUPP L) in accordance with the HSC Conflicts of Interest: Clinical Research policy. Please refer to the policy and SUPP L for further guidance on disclosure and submission requirements. FAQ guidance on this topic is also available.

59) Does the research involve (check all that apply):

For-profit sponsor or funding source? YES NO

Marketed drug, device, or other technology; or a drug or device, or other technology in development?
 YES NO

We are using amoxicillin / clavulanate as the study drug. This drug is generically available in the US. We are not seeking a new indication for this already FDA approved medication.

New technology, software, or therapeutic approach? YES NO

