William Beaumont Army Medical Center
Institutional Review Board

# HUMAN SUBJECTS RESEARCH PROTOCOL APPLICATION

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| **Version Date:** | **27 July 2016** |
| **Research Title:** | **Prospective Comparison of Sleeve Gastrectomy Outcomes with Different Stapling Devices** |
| **Principal Investigator:** | **LTC Eric Ahnfeldt, MC** |

**DIRECTIONS FOR FORM COMPLETION**:

1. Use this form for **all** new research project submission, and complete all sections of the form. **DO NOT REMOVE ANY OF THE TEMPLATED LANGUAGE OR MODIFY FORM.** Please be as complete and thorough as possible. Insufficient information may result in a delay in approving your project.

2. Submit this completed form along with all required supporting documents to the WBAMC Human Research Protection Office (HRPO) staff by email: usarmy.bliss.medcom-wbamc.other.dci--wbamc@mail.mil

3. You will receive confirmation via Outlook of receipt of your new protocol package by the WBAMC HRPO.

4. Contact the DCI HRPO anytime if you need any help, or if you have questions: 915.742.9502 or 915.742.6075.

## 1. GENERAL INFORMATION SECTION

**1.1 Protocol Title:** Prospective Study of Sleeve Gastrectomy Outcomes with Different Stapling Devices

**1.2 Principal Investigator**

Rank, Name, Corps: LTC Eric Ahnfeldt, MC, US Army
Title (PGY-[ ]): Attending
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 N. Piedras Street El Paso, TX 79920-5001
Phone Number: 915-742-4442
E-mail Address: eric.p.ahnfeldt.mil@mail.mil
CITI Training Date:
Role and responsibilities: Dr. Ahnfeldt will be responsible for overseeing the project, ensuring progress is made and that any required resources are made available. He may also be participating in the recruitment, consenting, and data collection. He will be one of the three staff surgeons that will be participating in the study.

**1.3 Sub-Investigators**

Rank, Name, Corps: CPT Daniel Roubik, MC, US Army
Title (PGY-[ ]): PGY-2
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
Phone Number: 615-238-7703
E-mail Address: daniel.j.roubik.mil@mail.mil
CITI Training Date: 25Feb2015
Role and responsibilities: CPT Daniel Roubik is a co-author of this study and is responsible for literature review, recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while they are in his possession. At the completion of the study, he will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Elizabeth Miller, MC, US Army
Title (PGY-[ ]): PGY-3
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
Phone Number: 915-742-4251
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CITI Training Date: 13May2015
Role and responsibilities: CPT Elizabeth Miller is a co-author of this study and is responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. She will carefully safeguard all documents, databases, and information while they are in her possession. At the completion of the study, she will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Jacob A. Swann, MC, US Army
Title (PGY-[ ]): PGY-3
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
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E-mail Address: Jacob.a.swann.mil@mail.mil
CITI Training Date: 28Jun2015
Role and responsibilities: CPT Jacob Swann is a co-author of this study and is responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. She will carefully safeguard all documents, databases, and information while they are in her possession. At the completion of the study, she will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Clay Merritt, MC, US Army
Title (PGY-[ ]): Resident PGY-2
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
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CITI Training Date: 20May2015
Role and responsibilities: CPT Clay Merritt is a co-author of this study and is responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while they are in his possession. At the completion of the study, he will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Eric Raschke, MC, US Army
Title (PGY-[ ]): Resident PGY-3
Service and Department: General Surgery
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Phone Number: 915-742-4250
E-mail Address: eric.t.raschke.mil@mail.mil
CITI Training Date: 16Feb2015
Role and responsibilities: CPT Eric Raschke is a co-author of this study and is responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while they are in his possession. At the completion of the study, he will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Aaron Lane, MC, US Army
Title (PGY-[ ]): PGY-2
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
Phone Number: 618-975-4461
E-mail Address: aaron.e.lane.mil@mail.mil
CITI Training Date: 22 June 2016
Role and responsibilities: Responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while they are in his possession. At the completion of the study, he will review all abstracts, oral

presentations, and papers for submission.

Rank, Name, Corps: CPT Yousef Abuhakmeh, MC, US Army
Title (PGY-[ ]): PGY-1
Service and Department: General Surgery
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Phone Number: 601-807-0588
E-mail Address: yousef.h.abuhakmeh.mil@mail.mil
CITI Training Date: 08 June 2016
Role and responsibilities: Responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while they are in his possession. At the completion of the study, he will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Joshua Dilday, MC, US Army
Title (PGY-[ ]): PGY-1
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
Phone Number: 314-604-1133
E-mail Address: joshua.c.dilday.mil@mail.mil
CITI Training Date: 07MAR2016
Role and responsibilities: Responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while they are in his possession. At the completion of the study, he will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Remigio Flor, MC, US Army
Title (PGY-[ ]): PGY-1
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
Phone Number: 305-505-5512
E-mail Address: remigio.j.flor.mil@mail.mil
CITI Training Date: 23 June 2016
Role and responsibilities: Responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while they are in his possession. At the completion of the study, he will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: CPT Barret Halgas, MC, US Army
Title (PGY-[ ]): PGY-1
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 North Piedras St. El Paso, TX 79920-5001
Phone Number: 936-524-7635
E-mail Address: barret.j.halgas.mil@mail.mil
CITI Training Date: 24 June 2016
Role and responsibilities: Responsible for recruitment, consenting, data collection, data analysis, and manuscript preparation. He will carefully safeguard all documents, databases, and information while

they are in his possession. At the completion of the study, he will review all abstracts, oral presentations, and papers for submission.

Rank, Name, Corps: LTC Jason Hiles, MC, US Army
Title (PGY-[ ]): Attending
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 N. Piedras Street El Paso, TX 79920-5001
Phone Number: 915-742-2282
E-mail Address: Jason.m.hiles.mil@mail.mil
CITI Training Date: 14 Dec 2015
Role and responsibilities: Dr. Hiles will be responsible for performing the surgery. He may also participate in the consenting process.

Rank, Name, Corps: COL (ret) John Schriver, MC, US Army
Title (PGY-[ ]): Attending
Service and Department: General Surgery
Current Duty Station/Address: William Beaumont Army Medical Center 5005 N. Piedras Street El Paso, TX 79920-5001
Phone Number: 915-742-2282
E-mail Address: john.p.schriver2.civ@mail.mil
CITI Training Date: 14 Dec 2015
Role and responsibilities: Dr. Schriver will be responsible for performing the surgery. He may also participate in the consenting process.

**1.4 Collaborating Staff/Non-Federal Collaborators**
N/A

**1.5 Research Monitor**

Rank, Name, Corps: Warren Alexander
Title (PGY-[ ]): Research Monitor
Service and Department: Hematology / Oncology
Current Duty Station/Address: William Beaumont Army Medical Center 5005 N. Piedras Street El Paso, TX 79920-5001
Phone Number: 915-742-2585
E-mail Address: warren.l.alexander.civ@mail.mil
CITI Training Date: Pending
Roles and responsibilities: Dr. Warren Alexander will serve as the research monitor for this study. In that role, Dr. Alexander will be an advocate for the subjects enrolled in this study. He will monitor the implementation of the project and provide an annual report to the IRB. He will complete any other tasks as required by the IRB.

**2. ABSTRACT (Summary)**:

Sleeve gastrectomy is now the most commonly performed bariatric surgery. While many studies have evaluated factors that may minimize post-operative hemorrhage and staple-line leak, we are unaware of any studies that compare outcomes between devices from the two main stapler manufacturers used in this surgery, Covidien and Ethicon. The purpose of this study is to compare intraoperative characteristics, such as time to create sleeve, intraoperative bleeding, and time needed to load each cartridge, and post-operative characteristics, such as any complication requiring readmission (leak or hemorrhage), further surgical intervention, and weight loss, between patients who underwent sleeve

gastrectomy with Covidien devices and Ethicon devices. Since we typically use the Ethicon device more frequently for this surgery due to cost, we want to test if one device is superior to another in clinical outcomes and use cost as a secondary metric. If one device has better clinical outcomes, it will be the preferred device regardless of cost. If neither proves superiority, we can justify using cost to determine which device to use in patient care.

**2.1 Key Words:**

Sleeve gastrectomy stapler Covidien Ethicon SEAMGUARD bariatric bleeding leak

**2.2 Purpose:**

The purpose of this study is to perform a non-industry-funded head-to-head comparison of endoscopic linear cutting staplers made by two different manufacturers, Covidien and Ethicon Endo-Surgery, Inc.

**2.3 Research Design:**

Prospective randomized single-blinded clinical study

**2.4 Methodology / Technical Approach** (**including the number of subjects/records to be studied**):

New bariatric patients who have elected for a sleeve gastrectomy as part of standard of care will be invited to participate in the study during the bariatric clinic at William Beaumont Army Medical Center. Patients who meet the inclusion criteria will be invited to participate in the study. Please see Section 6.2.3 for specific details on study recruitment and Section 6.2.4 for specific details on the consent process. These patients will be consented in the bariatric clinic by a research resident listed on the protocol.

Three folders will be made, one for each bariatric surgeon, and 25 Covidien cards and 25 Ethicon cards will be placed into each for a total of 150 patients. All bariatric surgeons are trained and familiar with both devices. Once consented, a card will be removed at random to determine which stapler will be used. Bioabsorbable staple line reinforcement will be utilized with both staplers. Once in the operating room, the case start time, time from first staple firing to completion of sleeve, total stapler loads required, number of staple misfires, character of any staple line bleeding, and time for tech to load each cartridge will be recorded on a data collection sheet by a research resident, listed as an associative investigator on this protocol. The subject's post-operative course will follow the bariatric protocol. During follow-up, they will be monitored for weight loss, post-operative complications, and any other required interventions. This information will be obtained by reviewing the subject's medical record after follow-up appointments. Per the bariatric protocol, subjects will follow-up as noted in 6.3.5. If a patient withdraws consent for the study prior to surgery, they will still receive surgery and perioperative treatment in line with institutional protocol, and they will be withdrawn and create a vacancy for a new subject. If a patient withdraws consent after surgery, we will cease logging data for the study on that subject. We will clarify whether they want all data to be removed from the study or if they simply want no more data to be entered into the study and abide by their wishes, and they will remain in the original randomized group in accordance with intention-to-treat principles.

**2.4.1 What is Standard of Care in this study?** ***(Standard of Care should be described in the Purpose section of the Consent Form. You should NOT list these in the Risk section of the Consent Form.)***
This study is looking at the comparative effectiveness of two FDA-approved devices, that are both well-described in the literature for this specific operation. These devices will be used in accordance with the labeling. Patients qualify for bariatric surgery if they have a BMI of 40 or 35 with obesity-related

comorbidities (hypertension, obstructive sleep apnea, pseudotumor cerebri, hyperlipidemia, diabetes, etc). All patients undergo psychiatric screening, laboratory assessment to rule out other cause of obesity, such as hypothyroidism, esophagogastroduodenoscopy, ultrasound of their gallbladder, and multiple counseling sessions prior to scheduling surgery. Patients may choose which bariatric procedure they prefer between sleeve gastrectomy, roux-en-y gastric bypass, and gastric band placement. Once scheduled for surgery, they will present to the hospital 6$^{th}$ floor. They will be given one dose of 5000 units subcutaneous heparin. Preoperative antibiotics of cefazolin or clindamycin will be administered within 30 minutes of surgery start time. Patients will be placed on the operating table in the supine position with a footboard in place. Sequential compression devices will be placed on the lower extremities. General endotracheal anesthesia will be induced. The abdomen will be prepped and draped in the usual sterile fashion. A time out will be completed, verifying the correct patient, procedure, site, positioning, and special equipment prior to starting the surgery. A fenestrated bougie will be placed through the patient's mouth, into the stomach. Pneumoperitoneum will be obtained, and a trocar with a laparoscope will be inserted. The abdominal contents will be inspected for evidence of injury. Three additional trocars will be placed under direct visualization and a Nathanson retractor will be used to retract the liver. Negative pressure will be applied to the fenestrated bougie after proper positioning laparoscopically. The stomach will be inspected, and a site 4-6 cm proximal to the pylorus will be identified. A defect will be made in the greater omentum at this site close to the greater curvature of the stomach using a harmonic scalpel. Dissection will be carried along the greater curvature of the stomach to the gastroesophageal junction, taking care not to injure the spleen. Starting with a black load with and absorbable polymer membrane reinforcement on either the Covidien iDrive with reinforced Tristaple technology or the Ethicon Echilon powered stapling device with Gore Seamguard reinforcement. Typically at our institution, the Ethicon Echilon device is used more frequently simply due to availability, but all bariatric surgeons are trained on both devices. Subsequent stapler loads will be surgeon and patient-dependent. Typically Ethicon black loads will be used until the fundus of the stomach, at which point a blue load without reinforcement is used. For Covidien, the black load is typically exchanged for a purple load near the fundus. Once the sleeve is complete, the stomach will be submerged in saline, and the remnant stomach will be insufflated, looking for any evidence of air leak, which would be repaired prior to conclusion of the case. The staple line will be inspected for bleeding. The gastric remnant will be removed though a port, and the abdomen will be desufflated. Incisions will be closed with 4-0 monocryl and covered in Dermabond. Patients are kept NPO and monitored overnight with intravenous fluids. They are started on water sips the next morning and are advanced to a bariatric liquid diet if they tolerated water sips. If they have adequate pain and nausea control and are taking in adequate fluid, they are discharged home on post-operative day one. They will follow-up at week 3, week 6, month 3, month 6, and annually.

**2.4.2 What is investigational or experimental in this study?** (***This is not Standard of Care. You will describe this in the Purpose section of the Consent Form, and MUST list these in the Risk section of the Consent Form. The risks should be listed as: Common; Probable; and Rare.)***

The stapler used for each surgery will be randomly assigned. Neither manufacturer has proven superiority, so there is no deviation from standard of care in using different staplers. Also, the data collection, including time to reload staplers, time to complete sleeve, documentation of staple line bleeding, post-operative complications, and weight loss, is unique to this study and be recorded in a spreadsheet unique to this project.

**2.4.3 Is any part of the investigational / experimental procedure(s) you are doing Off-Label Use?** *(If the answer is yes, you must discuss the Off-Label Use with the HPA / RRS).*

No

**3. OBJECTIVES AND SPECIFIC AIMS**:

Primary objectives: Determine if using different brand staplers affects:

1. Time of creation of sleeve from first firing to completion
2. The percent of firings with technical difficulties
3. The time for tech to load each staple cartridge (aware of Hawthorne effect. Since both arms will be subject to Hawthorne effect, the only variable should be the stapler)

Secondary objectives: Determine if using different brand staplers affects:

1. Any bleeding after creation of the sleeve (annotating whether single or multiple interventions are required)
2. Weight loss
3. Leak rates
4. Hospital readmissions or emergency room visits (For complications including but not limited to dehydration, hemorrhage, leak, internal hernia, and pain; will annotate what complication warranted readmission)
5. Further sleeve interventions

**4. MEDICAL APPLICATION/ MILITARY RELEVANCE**:

Bariatric surgery is very common in military treatment facilities with surgical capability. Determining if a certain stapler is superior has potential to reduce complication rates, improve quality of care, decrease costs, and optimize resource utilization.

## 5. BACKGROUND AND SIGNIFICANCE SECTION

**5.1 Literature Review and Preliminary Data and/or Findings**:
Demonstrate that you have done a comprehensive literature search that includes the following:

**a. Date of Search**: 02 Sept 2015

**b. Search terms used**: Laparoscopic sleeve gastrectomy, stapler, bariatric surgery, Covidien, Ethicon

**c. Databases Searched**: PubMed, Google Scholar

In 2011 and 2012, it was found that 34.9% of Americans were obese [1]. As a result, many patients will turn to bariatric surgery to assist with weight loss and resolution of obesity-related comorbidities. The three most commonly utilized bariatric procedures are the roux-en-y gastric bypass (RYGB), adjustable gastric band placement, and sleeve gastrectomy. While the RYGB was historically the most commonly performed procedure, laparoscopic sleeve gastrectomy is rapidly gaining popularity, accounting for 0.9% of bariatric procedures in academic centers in 2008 to 36.3% in 2012 [2]. According to the American Society for Metabolic and Bariatric Surgery (ASMBS), laparoscopic sleeve gastrectomy is now the most commonly performed bariatric surgery in the United States as of 2013 [3].

Sleeve gastrectomy was first described as part of a biliopancreatic diversion with duondenal switch in 1998 and was performed laparoscopically in 1999 [4,5]. It was first done as a stand-alone procedure in 2003 as part of a two-stage weight loss procedure and was recognized by the ASMBS as an acceptable option for primary bariatric surgery in 2009 [6,7]. The procedure is most commonly performed using a linear cutting stapler to form the gastric sleeve. The most concerning complications from this procedure include staple-line leak and hemorrhage, which occur in 2.8 and 3% of patients overall, respectively [8]. Multiple studies have been conducted to determine how to reduce complication using staple line analogs, such as oversewing with suture, using bovine pericardium, applying liquid hemostatic matrices, and using an absorbable polymer membrane (GORE SEAMGUARD Reinforcement, W. L. Gore & Associates, Elkton, MD) [9,10,11]. In a recent study, the absorbable polymer membrane was found to have lowest leak and overall complication rate [12].

There are two main manufacturers of laparoscopic linear cutting staplers that are Food and Drug Administration-approved for use in laparoscopic sleeve gastrectomies, and both have options for absorbable polymer membrane reinforcement. These companies are the Covidien with iDrive™ Ultra Powered Stapling System and Endo GIA™ Reinforced Reload with Tri-Staple™ Technology (Covidien, Dublin, Ireland) [13] and Ethicon with the Echelon™ Stapler (Echelon Flex™ Powered Endopath® Stapler; Ethicon Endo-Surgery Inc., Cincinnati, OH, USA) [14], which is compatible with GORE SEAMGUARD for reinforcement [15]. While a study with 26 patients incidentally found no difference in outcomes between the two devices without an absorbable polymer membrane [16], to our knowledge there is no non-industry-funded study designed to compare intra-operative findings and outcomes in sleeve gastrectomy between the two devices with absorbable polymer membranes. We hypothesize that the sleeve creation time and time needed to load each staple cartridge will be different between the two devices

**5.2 Scientific Justification:**

Linear cutting staplers function by firing six rows of staples and then cutting with three on each side. Depending on the manufacturer, the staple height and method of firing differs. The staple height affects the ability to achieve hemostasis and tissue approximation. Currently there are two manufacturers of such FDA-approved devices, neither of which has any proven superiority for sleeve gastrectomies. This study would help us decide if we can provide better patient care by using a particular device.

**5.3 Human Use Justification:**

This research involves no deviation from standard of care for a common human surgery. In order to fairly assess outcomes in human patients, the data must be from human subjects.

## 6. PLAN SECTION

**6.1. New Investigational Drugs/ Investigational Devices Exemption Status:**

N/A

**6.1.1. Exemptions for an Investigational New Drug (IND) application to the FDA:**

N/A

**6.1.2. Studies under an Investigational Device Exemption (IDE) or are Exempt from an IDE Requirement:**

N/A All devices in the study are already FDA approved for the intended study purpose. Please see 510K and labeling information included with the submission.

**6.2 Selection of Subjects**

**6.2.1 Type of the Subject Population:**

New bariatric patients who have already opted to pursue a sleeve gastrectomy will be invited to enroll in the study in the bariatric clinic during their pre-operative visit.

**6.2.2 Inclusion and Exclusion Criteria**

**a. Inclusion Criteria *(justify the inclusion of subjects who may be vulnerable; i.e., pregnant women, children, decisionally impaired that require proxy (LAR) consent, enlisted Soldiers, etc.)***

a. Informed consent obtained and signed from each subject,
b. Age ≥ 18 years
c. Requirement for agreement to avoid conception
d. BMI >40
e. BMI >35 with obesity-related co-morbidity
f. Pre-operative psychiatric evaluation
g. Pre-operative laboratory studies that fail to demonstrate secondary cause of obesity
h. Pre-operative upper endoscopy performed with biopsy
i. Full course of triple therapy for patients with *Helicobacter pylori* on EGD

**b. Exclusion Criteria *(Explain if a specific population is being excluded and provide a justification for doing so)***

a. Pregnancy- Patients are not eligible for bariatric surgery, and if they become pregnant after surgery, they would present confounding variables and alter weight loss
b. Tobacco use within one month of surgery or any time within study period- Most staff will not perform bariatric surgery on active smokers as it negatively impacts healing
c. Prior bariatric surgery- Makes repeat bariatric surgery more difficult and could increase risk of complications
d. Inflammatory bowel disease- Rare diagnosis that may increase chance of complications, thus confounding results
e. Active duty military- Not eligible for bariatric surgery

**6.2.3 Recruitment**

**a. Subject selection must be equitable*; i.e., male/female, age range, racial and ethnic origin***:

Subjects will be selected and randomized into each group without discrimination by gender, race, or ethnicity. A predominantly female population is expected based on the historical patient population for bariatric surgery.

**b. Describe method of screening subjects and indicate <u>when</u>, <u>where</u> and <u>how</u> study subjects will be recruited, if applicable**:

For a bariatric patient to make it to their appointment to schedule their surgery, they will have already been screened as part of standard of care. This screening includes: ensuring BMI and comorbidities meet requirements to qualify for surgery, laboratory tests looking for an organic cause of obesity, psychiatric evaluation, upper endoscopy with gastric biopsies, ultrasound of the gallbladder if present, and several counseling sessions. Once all requirements have been met, they are seen in the bariatric clinic. Patients may choose which bariatric procedure they desire based on the information provided at the educational conferences without any coercion by staff to pick one procedure over another for research purposes. The educational conference is standardized and will not change as a result of implementation of this study. Staff may recommend the gastric bypass to certain patients based on excessive BMI or comorbidities, but the patient ultimately decides which surgery they desire based on all the information they are provided. When a patient had elected for a sleeve gastrectomy, he/she will be invited to speak with a research resident listed on the protocol , and a flyer pertaining to the project will be available for the patient to arrange a meeting to discuss the project. The research project representative will meet the patient, and details of the study will be discussed in person with patient. Pertinent topics of discussion will be that two different companies manufacture FDA-approved devices that are used for sleeve gastrectomies. Neither has been proven superior, and the aim of this study is to see if our institution has better results with one particular device in an effort to improve future patient care. The patient will be seen the day of surgery by a research representative, and he/she will be able to opt in or out at that time if they desire.

**c. Compensation for participation**:

None

**6.2.4 Consent Process**

**a.** ***Discuss <u>how</u> and <u>when</u> subjects will be consented, <u>who</u> will administer consent/HIPAA authorization and steps taken to prevent coercion.***

Patients will be consented in person and sign a written consent during their bariatric pre-operative visit or at a later time if the patient so chooses. The consent process will be performed by a research physician. Patients may opt out of the study at any time. All patients will be consented individually in a private space at their convenience. Any questions related to the study will be answered prior to signing the consent form.

**b.** ***Discuss efforts made to promote subjects' understanding of the consent form:***

Patients will have already gone through extensive counseling on the surgeries as part of the department protocol. As this study looks at a part of the surgery that would occur without the study, they will already be familiar with the surgery. However, the details will be discussed again with the patient. A written consent will also be available. Someone is available to answer questions at any time. The patient will be seen the day of surgery by a research representative, and he/she will be able to opt in or out at that time if they desire.

**c.** ***Justify Waiver of Consent/Waiver of HIPAA Authorization, Waiver of Documentation of Consent (consent without signature), if applicable:***

N/A

**6.3 Study Design and Methodology - As appropriate, the study design and methodology should include the following sub-sections.**

**6.3.1 Study Design Statement –** ***Describe in detail the type of study design including description of randomization/blinding and how any confounding variables will be controlled by study design:***

**a. Describe what will happen on this study that is RESEARCH/EXPERIMENTAL:**

Subjects will be randomly assigned to one of two devices as they are scheduled for surgery using a shuffled stack of cards. Despite being the same operation that would be performed without the study, data will be collected throughout the case and recorded for research purposes as mentioned above.

**b. Describe what will happen on this study that is STANDARD of CARE:**

All elements of this study abide by the standard of care. Up to this point, there's been no proof that one stapler brand is superior to the other, so using either stapler is current standard of care. Both devices are currently used at WBAMC. Currently, the Ethicon Echilon is more frequently used due to availability, but all bariatric surgeons are trained and comfortable with the Covidien iDrive. Subjects will have the same pre-operative work-up as described previously, they will undergo the same operation, and have the same post-operative care, medications, and follow-up as each other and their counterparts not enrolled in the study.

**6.3.2 Study Methodology/Procedures:**

Patients who express an interest in bariatric surgery will attend a bariatric seminar and initiate the process of scheduling bariatric surgery per department protocol. Once qualified for surgery, the patients will present to bariatric clinic, which takes place in the general surgery clinic on Tuesdays, and have a one-on-one discussion about their desired surgery with a staff physician. If the patient desires a sleeve gastrectomy, the study will be discussed. Consent will be obtained, and the patient will be randomized into the Covidien or Ethicon group. The subject will proceed with surgery per department protocol. In the operating room, a data collection sheet will be available in the operating room to make note of time for creation of sleeve from first firing to completion, total number of staple loads fired, number of misfires, character of any bleeding at the staple line and which interventions were required to control it, and time it takes for the surgical technologist to reload the stapler. At William Beaumont surgical technologists are trained on loading each linear cutting stapler by the Covidien and Ethicon representatives. We will still ensure at the start of the case they are familiar with loading the provided device. No additional training for device will be mandated, as surgical technologist turnover would make this difficult to provide equal training, and it would detract from internal and external validity, since we do not normally provide extra training. Typically the sleeve is created by staff or higher level residents (PGY-2 and above). However, all residents are trained on the devices and are therefore capable of creating the sleeve with close staff supervision, as is standard for our institution. For the purpose of this study, we intend on maintaining this practice since all level residents may be assisting and performing this surgery throughout their residency and deviation would lead to questionable internal validity. After surgery, patients will be admitted to the hospital, and care will follow the department's bariatric protocol. Once discharged, they will follow-up at 3 weeks, 6 weeks, 3 months, 6

months, and then annually. Subjects will be followed for 1 year after surgery. During that time, weight loss, presence of staple line leaks, any readmissions, and any other interventions will be monitored.

**6.3.3 Prospective Collection of Human Biological Specimens:**

No additional biological specimens will be obtained or banked exclusively for the purposes of this study.

**6.3.4 Data Collection (*all study variables/instruments/questionnaires to be administered*):**

There will be two separate data logs maintained for the purposes of this study. The first log (master key) will contain all subject identifiers and PHI. Specifically, the master key will include:

- Patient identifier (to be linked to study log)
- Patient name
- Date of birth
- Surgeon
- Date of operation
- Family member prefix with last four digits of the social security number

The second log (data collection sheet) will include patient identifier to link to master key, but include no other PHI or direct identifiers. A data collection sheet that omits identifiable patient health information (only a pre-assigned identifier unique to the study) will be present in the operating room. This information will be transcribed to a data log on a secure computer. Specifically, the data collection sheet will include;

- Patient identifier (to link to master key)
- Gender
- Race
- Age
- Pre-operative height (needed to calculate ideal body weight)
- Pre-operative weight
- Intra-operative data points, to include time to load stapler, time to create sleeve, intra-operative bleeding or leak, and number of staple load misfires
- Weight recordings from follow-up appointments
- Annotations of any re-admissions or complications after surgery
- Follow-up weight (at follow up points)
- Weight loss (at follow up points)
- Need for hospital readmission or emergency room visits with annotation of the complication that caused the increased need for hospital care

A research resident listed on the protocol will be present during the operation to populate the data points on the data collection sheet. Timing, done by a physician, will require a stopwatch to monitor the total sleeve creation time and the time it takes to load each stapler cartridge. This data will be transcribed into the Excel data collection spreadsheet on a secure, password-protected computer. Data from follow-up visits, such as complications and weight, will be acquired via chart review through AHLTA and CHCS. The master key with patient identifiers will be linked to the data log sheet to allow physician researchers to acquire this information from the electronic medical records. All information will remain on a secure hospital computer and will be intermittently updated by a research resident as the study progresses. As listed above, information acquired from chart review during this study will include: follow-up weight, weight loss, and need for hospital readmission or emergency room visits with annotation of the complication that caused the increased need for hospital care. Other information, such as name, height, race, age, family member prefix with last four digits of the social security number, initial weight, surgeon, date of the operation, data points collected in the operating room (time to load stapler, time to create sleeve, intra-operative bleeding or leak, and number of staple load misfires) will

have already been added to the list shortly after the patient's procedure.

**6.3.5 Study Time Line *(provide diagram or table that outlines sequence/timing of study procedures)*:**

| Assessment | Visit/follow-up interval relative to surgery | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time period | >1 month pre-op | <1 month pre-op | Day of surgery | Post-op day 1 | Post-op week 3 | Post-op week 6 | Post-op month 3 | Post-op month 6 | Post-op year 1 |
| Height/Weight | X | X | X | X | X | X | X | X | X |
| Pre-op bariatric work-up (counseling, labs, endoscopy, ultrasound, psychiatric evaluation) | X | | | | | | | | |
| History and physical | | X | | | | | | | |
| Schedule surgery | | X | | | | | | | |
| Consent/Counseling on study | | X | | | | | | | |
| Randomization | | X | | | | | | | |
| Deidentification and population of secure data sheet | | X | X | X | X | X | X | X | X |
| Pre-op labs (CBC, pregnancy test, renal panel, type and screen) | | X | | | | | | | |
| Measure time for sleeve creation (sec) | | | X | | | | | | |
| Measure total stapler loads fired | | | X | | | | | | |
| Measure number of loads fired with technical difficulties | | | X | | | | | | |
| Record staple line bleeding and hemostatic interventions | | | X | | | | | | |
| Record time to load each staple cartridge | | | X | | | | | | |
| Labs | X | X | | X | | | | X | X |
| Assess for adverse events | | | X | X | X | X | X | X | X |

**6.3.6 Dissemination plan to publish and/or present results of this research:**

Data will be collected and interpreted with the goal of publication in a medical journal and presentation and national conferences

**6.3.7 Has any other Scientific Review Committee/Organization reviewed this project for scientific merit? Yes [ ] No [x]. If yes, name the organization, year, and merit/score:**

**6.4 Statistical Consideration.**

**6.4.1 Statistical hypothesis, primary endpoints (i.e., primary outcome variables), and secondary endpoints, if any:**

Research Hypothesis: As a superiority study, the research hypothesis is Ethicon linear cutting staplers with staple line reinforcement will have different outcomes when performing laparoscopic sleeve gastrectomy when compared to Covidien staplers with staple line reinforcement.

Primary objectives: Determine if using different brand staplers affects:

1. Time of creation of sleeve from first firing to completion
2. The percent of firings with technical difficulties
3. The time for tech to load each staple cartridge (aware of Hawthorne effect. Since both arms will be subject to Hawthorne effect, the only variable should be the stapler)

Secondary objectives: Determine if using different brand staplers affects:

1. Any bleeding after creation of the sleeve (annotating whether single or multiple interventions are required)
2. Weight loss
3. Leak rates

4. Hospital readmissions or emergency room visits (For complications including but not limited to dehydration, hemorrhage, leak, internal hernia, and pain; will annotate what complication warranted readmission)
5. Further sleeve interventions

**6.4.2 Data analysis:**

For the continuous primary endpoints, the two-sample t-test for 2 means will be used to compare the 2 Devices at Surgery. For the continuous secondary endpoints, such as weight loss, the General Linear Mixed Model Analysis for repeated measures over time will be used to test for the Device effect, Time effect and the Device by Time Interaction. For the binary secondary endpoints (Yes/No), such as Staple line leak, Readmission or ER visits, further sleeve interventions, over time, the General Estimating Equations (GEE) analyses will be used to test for Device effect, Time effect and the Device by Time Interaction. For all tests, the level of significance is set at 0.05.

**6.4.3 Sample Size Estimation:**

75 in each arm for a total of 150 patients. The preliminary power analysis indicated 64 in each arm to be sufficient, to be able to detect a medium effect size of 0.5 for the two-sided t-test, with $\alpha = 0.05$ and 80% power, so 11 extra patients per arm have been added for attrition. The power analysis was based on the research hypothesis of a difference in the 2 devices, with this superiority study using time to create sleeve as the primary variable.

**6.4.4 Safety Monitoring and Analysis Plan:**

Complication rates in each arm will be monitored as the study progresses. Across the nation, each stapling device is used with no study demonstrating superiority or inferiority. Therefore, no extraneous risk is expected to be put on patients as a result of this study. As they arise, adverse events will be documented in the Excel spreadsheet used for longitudinal data collection. If significant differences in complications or patient outcomes arise before study completion (one device proves to be safer), the study will be aborted, and the paper will be published with the data available. Patients will be notified over the phone or in person if the study is concluded early with an explanation of the reasoning.

**6.4.5 Will the results of this research be submitted to the Food and Drug Administration (FDA) for marketing approval? [x] No [ ] Yes** (If "Yes" provide a memo with detailed information regarding the submission to the FDA )

**6.5 Risks, Benefits and Adverse Event Reporting**

**6.5.1. Risk/Benefits:**

**a. Risks to subjects:** Risks of this trial are similar to those in patients receiving a laparoscopic sleeve gastrectomy who are not enrolled in the trial. They include: pain, infection, bleeding, damage to surrounding structures, such as but not limited to spleen, esophagus, pancreas, liver, and intestines, stricture of the sleeve, need to convert to open procedure, nausea, vomiting, leak of the staple line, and inherent risks of prolonged anesthesia, such as blood clots in the legs that can travel to the lungs, stroke, heart attack or death. These risks are all specific to the procedures that will be taking place as part of standard of care and are not specific to the research study.

There is also a slightly increased risk of breach of confidentiality, which is specific to the research study. To minimize this, the only research-related document that has patient identifiers with study information will be on a secure computer.

**b. Benefits to subjects:** Patients who undergo a sleeve gastrectomy and modify lifestyle accordingly typically lose around 60% of their excess body weight. Some patients may also note improvements in their blood pressure, blood sugar levels, and cholesterol. If one stapler is found to be superior, patients may experience improved outcomes and/or fewer complications. Currently at WBAMC, the large determining factor on device utilization is financial. By having clinical justification for using one particular device, it demonstrates our eagerness to put the patient first.

**c. Precautions to mitigate risks:** All physicians have undergone training with both stapling devices to be used in this research study. Other than the stapler and bioabsorbable staple line reinforcement that will be used, there should be no variation in technique between the two study arms. Post-operative care will follow the department protocol, which involves monitoring patients for at least one night for complications. They will follow-up in clinic several times post-operatively to ensure patient has all needs and concerns addressed. The data collection sheets that are in physical circulation will have a deidentified code that can only be associated with a patient once entered into the secure Excel spreadsheet that is used for longitudinal data collection. In this way, it would be impossible to get personal patient information without being on a hospital computer approved for use of electronic medical records.

**6.5.2 Expected Adverse Events from Research Risks and Reporting:**

Overall, the risk of complications from sleeve gastrectomy generally falls in the less likely range (1%-5%). According to other studies that have been performed using both staplers, they did not report significant differences in staple line leaks. [16] Additional risks as a result of this study are expected to fall in the rare but serious range (<1%). Such risks may include minor staple line bleeding which will be addressed in the operating room, which may be attributed to a surgeon using one stapling device less than another despite being fully trained for both. Post-operative staple-line leak, pain, dehydration, infection, and blood clots are also known complications of the surgery, but the study is not expected to alter the likelihood of these events.

**6.5.3 Plan for Reporting Serious and Unexpected Adverse Events to the IRB:**

Serious adverse events- The PI will report all serious adverse events occurring in subjects enrolled to the William Beaumont Army Medical Center IRB within 2 working days of the discovery of the adverse event. An internal adverse event report memorandum will be submitted to the IRB/DCI.

Unexpected (but not serious) adverse events, which, in the opinion of the PI, are possibly related to participation in the protocol, will be reported by the PI within 30 days of the IRB.

For all serious and/or unexpected adverse events the PI will forward a copy of the adverse event report to the IRB.

**6.6 Human Biological Specimens/Tissue (HBS/tissue) Storage for Future Use:**

N/A

**6.7 Subject Confidentiality Protection:**

**a. Precautions to protect confidentiality of research records?**
Describe precautions you will take **(*physical/electronic/unique identifiers***) to protect the confidentiality of research source documents (Case Report Forms, questionnaires, etc.), research data file, and master code (if any)?

Once patients are enrolled in the study, their name and date of birth will be entered into an Excel spreadsheet (master key), and subjects will be assigned unique identifiers that will be used throughout the study. All authors and co-authors in the study will have access to the spreadsheet. Physical data collection sheets that will be available in the OR will only have the unique identifier. Once the information has been transcribed into the spreadsheet, the physical data collection sheet will be shredded. The spreadsheet will be maintained on a hospital computer that is password protected and requires a Common Access Card to log in.

**b. Who** will be responsible for ensuring research records are secured prior to destruction date?

Daniel Roubik will maintain the data sheets on a secure computer until completion of the study

**c. Destruction plan for research records?**
**When** and **how** will the research documents, data files, and the master code be destroyed?

The physical data collection sheets will be placed into a hospital shred bin once information has been entered into the digital spreadsheet. Once all data collection, analysis, and publication is complete, the spreadsheet with patient identifiers will be modified to eliminate any identifiable information (name, date of birth, and date of operation), and the document will be maintained on a secure hospital computer for at least 3 years, at which point the file will be deleted.

**6.7.1 Certificate of Confidentiality:**

N/A

**6.7.2 Health Insurance Portability and Accountability Act (HIPAA) and Identifiable Protected Health Information**

**a. Access (visible PHI during data collection), Use, and/or Collection of Any PHI?**

**Mark 'Yes' if a Study Staff Member will have Direct Access To, Use, and/or Collect (i.e., record in dataset) any of the following 18 personal identifiers (PHI)!**

**[x] Yes - Check ALL that apply:**

[x] 1. Names
[ ] 2. Street address, city, county, 5-digit zip code
[x] 3. Months, dates (years are OK), ages >89 (unless all persons over 89 years are aggregated into a single category)
[ ] 4. Telephone numbers
[ ] 5. Fax numbers
[ ] 6. E-mail addresses
[x] 7. Social security number
[ ] 8. Medical record number
[ ] 9. Health plan beneficiary number
[ ] 10. Account number
[ ] 11. Certificate/license number
[ ] 12. Vehicle identification number (VIN) and/or license plate number
[ ] 13. Device identifiers and serial numbers
[ ] 14. URLs (Uniform Resource Locators)
[ ] 15. Internet protocol address number
[ ] 16. Biometric identifiers, such as finger and voice prints
[ ] 17. Full face photographic images or any comparable images
[ ] 18. Any other unique identifying number, characteristic, or code such as patient initials:
**_____(Provide Unique Identifier)**

**Mark 'No' if Study Staff Members will NOT have Direct Access To, Use, and/or Collect (i.e., Document in dataset) any of the 18 personal identifiers (PHI) listed above!**

**[ ] No - Study investigators will NOT see, use, or record any PHI - HIPAA regulations do not apply; however, precautions for research records must still be described above 6.7).**

**b. Limited Data Set?**

Can you limit your collection of personal identifiers to just dates, city/state/zip, and/or "other unique identifier" (#18 of the above)?

**[ ] Yes** – then your dataset may qualify as a Limited Data Set – complete the Data Use Agreement (2.i).

**[ ] No**
**[x] N/A**

**c. Sharing research data, with or with the inclusion of PHI, outside of WBAMC?**

Will research data including Identifiable Protected Health Information be sent outside of WBAMC?

**[ ] Yes** – **Obtain Business Associates Agreement,** explaining assurances you have received from the outside party that they will appropriately follow confidentiality protections, follow the HIPAA requirements, and abide by the provisions of your Authorization.
**[ ] No**
**[x] N/A**

**6.7.3 Waiver of HIPAA Authorization Request?**
If you wish to obtain and use identifiable PHI (protected health information) for a study without obtaining written approval ("HIPAA Authorization") from the subject, complete the HIPAA Waiver of Authorization Template and provide justification for IRB review and approval.

a. **Justify why obtaining subject Authorization is "impracticable"? (i.e., *minimal risk research plan, adequate plan to protect identifiers from improper use and disclosure, adequate plan to destroy identifiers at earliest opportunity, written assurance that PHI will not be reused or disclosed?)***

b. **Is the PHI being collected the minimum necessary for this research**?
**[ ] Yes [ ] No [x] N/A**

**6.7.4 Partial Waiver of HIPAA Authorization for recruitment purposes?**
If you must review patient charts, clinic visit logs, or other source documents to determine subjects eligible for your study, complete the Partial Waiver of HIPAA Authorization Template and provide justification for IRB approval
**[ ] Yes [ ] No [x] N/A**

**6.8 Plan for Reporting Protocol Deviations:**

Minor deviations are defined as minor administrative, procedural or scheduling changes to accommodate subject comfort that do not affect the scientific soundness of the research plan or the rights, safety, or welfare of human subjects. Minor deviations will be reported in the progress report at the time of continuing review. Any deviation that does not meet the definition of a minor deviation is considered a major deviation. Major deviations will be reported to the WBAMC Chief, DCI and HPA within 72 business hours of discovery both verbally and in writing.

## 7. REFERENCES SECTION


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5. Ren, C. J., Patterson, E., & Gagner, M. (2000). Early results of laparoscopic biliopancreatic diversion with duodenal switch: a case series of 40 consecutive patients. *Obesity Surgery*, *10*(6), 514-523.
6. Regan, J. P., Inabnet, W. B., Gagner, M., & Pomp, A. (2003). Early experience with two-stage laparoscopic Roux-en-Y gastric bypass as an alternative in the super-super obese patient. *Obesity surgery*, *13*(6), 861-864.
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laparoscopic sleeve gastrectomy: a multicenter study. *Surgery for Obesity and Related Diseases*, *10*(3), 450-454.
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## 8. OTHER IRB REVIEW SECTION

N/A

## 9. FACILITIES/ORGANIZATIONS TO BE USED

**If 'yes' to any of the below listed Departments, Services, Wards and/or Clinics, obtain impact statement from that department.**

**Inpatient Wards/Units/Clinics**: [x] No [ ] Yes

**Nursing**: [x] No [ ] Yes

**Pathology**: [x] No [ ] Yes

**Pharmacy**: [x] No [ ] Yes

**Radiology**: [x] No [ ] Yes

**RPO Statement [Protocol involves extra radiation]:** [x] No [ ] Yes

**Clinical Investigation**: [x] No [ ] Yes

**Other Department /Service: (please identify)** [x] No [ ] Yes

## 10. TIME REQUIRED TO COMPLETE THE RESEARCH (INCLUDING DATA ANALYSIS).

**10.1 Anticipated start date:** 31 August 2016

**10.2 Expected completion date:** 31 March 2018

## 11. FUNDING SECTION

**WHAT FUNDING IS NEEDED TO SUPPORT THIS PROTOCOL?**

| | |
|---|---|
| **[x] No funding needed.** | |

| | |
|---|---|
| **[ ] Non-Federal funding/resources** | Provided via Cooperative Research and Development Agreement (CRADA) and Statement of Work (SOW) between Sponsor and Clinical Investigation Regulatory Office (CIRO) |
| **Name of Sponsor**:<br>**Name of Foundation (if used)***:<br>**Foundation POC & Phone #**:<br>* if no Foundation is used, see DCI for help in creation of CRADA, required to collaborate with sponsor. | |

| | |
|---|---|
| **[ ] Federal funding/resources via MIPR** | **Source:** |
| | |
| **[ ] Request funding/resources from investigator's department** | Department/Service level funding requires impact statement signed by the respective Department/Service chief. |

| | |
|---|---|
| **[ ] Request funding/resources from DCI**<br>For consumable supplies, equipment, or other costs attach a separate page itemizing needed items, estimated cost, source, and quantity | Funding from DCI generally does not exceed $2,000 per fiscal year. If funding exceeds approved amount, a funding amendment will have to be requested by memorandum through DCI and/or the IRB. |

| | |
|---|---|
| **[ ] Request funding for Presentation**<br><br>Clearance of presentation is required prior to submission | A funding request for travel may be approved for protocols. Funding is contingent on availability of funds. The source of funds is GME account. Priority goes to Residents, Fellows, and Interns. Others are considered on a case-by-case basis.<br><br>NOTE: Only ***one*** funded TDY ***per protocol*** for an investigator. |

| | |
|---|---|
| **[ ] Request funding for Publication**<br><br>Clearance of publication is required prior to submission. | This funding covers the cost of publishing an article and reprints. **Publication is highly encouraged**. |

## 12. ENVIRONMENTAL IMPACT STATEMENT

**Does any part of this protocol generate any of the following regulated waste?**

| | |
|---|---|
| **a. Hazardous Chemical Waste** | **Yes ( ) No ( x )** |
| **b. Regulated Medical Waste** | **Yes ( ) No ( x )** |
| **c. Radioactive Waste** | **Yes ( ) No ( x )** |

## 20. Protocol Document Submission Checklist

**Upload each of the following documents, as appropriate for your study.**

| | |
|---|---|
| **[ ]Current Protocol Template**<br>**[ ]Master Protocol**<br>**[ ]Main protocol sites approval letter (if a local Multicenter)**<br>**[ ]NCI (National Cancer Institute) CIRB (Central IRB) Approval Letter**<br>**[ ]Waiver of Consent**<br>**[ ]Waiver of Documentation of Consent**<br>**[ ]Waiver of Authorization (HIPAA)**<br>**[ ]Partial Waiver of HIPAA Authorization for screening/recruitment**<br>**[ ]Consent Form(s)/HIPAA Authorization Addendum**<br>**[ ]Assent Form**<br>**[ ]Model Consent from the main protocol site**<br>**[ ]Data Use Agreement**<br>**[ ]Flyers/[ ] Posters/[ ] Advertisements**<br>**[ ]Subject Handouts**<br>**[ ]Questionnaires/Surveys**<br>**[ ]Pain Scales**<br>**[ ]Data Collection Sheets** | **[ ]FDA Form 1572**<br>**[ ]Sponsor's Investigational New Drug (IND) Exemption Letter**<br>**[ ]FDA IND Letter or Number**<br>**[ ]Investigator Drug Brochure**<br>**[ ]FDA Expanded Access Letter/Approval**<br>**[ ]Approved Device/Drug Information Sheets (package insert)**<br>**[ ]Sponsor's Non-Significant Risk (NSR) Letter**<br>**[ ]Device Brochure**<br>**[ ]FDA 510(k) Letter with Indications for Use**<br>**[ ]FDA Investigational Device Exemption (IDE) Letter (complete and un-redacted)**<br>**[ ]FDA Pre-Market Approval (PMA) Letter**<br>**[ ]FDA Treatment Use Letter**<br>**[ ]Inclusion/Exclusion Checklist**<br>**[ ]Screening Log**<br>**[ ]Case Report Forms**<br>**[ ]Signed Letters of Support (for protocols involving Soldiers outside of WBAMC)** |

**[ ] ALL signed Impact Statements (ensure ALL Impact Statements are completed correctly and signed for this study):**

- **[ ] Pathology Impact statement**
- **[ ] Pharmacy Impact statement**
- **[ ] Nursing Impact statement -**
- **[ ] Radiology Impact statement**
- **[ ] Radiation Protection Committee (only if EXTRA, other than SOC radiation is involved)**
- **[ ] DCI Impact statement**
- **[ ] Other Impact statement**

If an Investigational New Drug (IND) study, provide the signed original of the FDA Form 1572 (Statement of Investigator) and/or FDA Form 1571 (if PI is the IND Applicant). The FDA Forms are at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html.