Endostapler Study Protocol

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A proposed study using AEON™ Endostapler Handles and Reloads

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SUMMARY

The goal of this prospective, post-market study is to measure AEON™ Endostapler performance for laparoscopic bariatric surgery against the Endo GIA™ Reloads with Tri-Staple™ Technology from Medtronic. Stapler performance will be evaluated primarily by incidence and degree of staple line bleeding from endoscopic images, evaluated by a blinded third-party. The study will include 60 total consecutive cases of individuals undergoing a planned laparoscopic sleeve gastrectomy (LSG). The LSG procedure will be performed according to institutional standard-of-care and all subjects will undergo standard preoperative evaluation as well as post-operative care. Relevant data will be collected using the Data Collection sheet which should be filled out following each procedure by a member of the surgical or nursing team.

Enrollment: 60 Subjects Meeting Inclusion/Exclusion Criteria

Investigator Masking: None (Open Label)

Primary Outcome Evaluator Masking: Yes (Surgeon and Device)

Devices: AEON™ Endostapler and Endo GIA™ Reloads with Tri-Staple™ Technology and Ultra Universal Handle

BACKGROUND

The AEON™ Endostapler is comprised of a stapler handle and reloads. The handle may accept multiple reloads of single fire cartridges. The AEON™ Endostapler devices were approved by the United States Food and Drug Administration (FDA) under the 510(k) process. Pertinent applications numbers are K171589 and K173443. Devices will be used pursuant to the indications specified in K171589 and K173443, as well as the general guidelines for use of this device on a prescription basis as outlined by the Federal Food, Drug, and Cosmetic Act (1976), and the Code of Federal Regulations Title 21 Part 800-895.

Approved Indications for Use

The AEON™ Endostapler has applications in general, abdominal, gynecologic, pediatric and thoracic surgery for resection, transection and creation of anastomoses.

Available AEON™ Endostapler Reloads

The following two tables contain the available AEON™ Endostapler Reloads, as well as the similar products that they may replace. This is meant as a guide, and the surgeon should read and follow the Instructions for Use and use their own clinical judgment to determine appropriate products to use.

Table 1. Available AEON™ Endostapler Reloads

Reload Type	Cartridge Length	Product Code	Open Staple Height	Closed Staple Height	Minimum Port Size
Gray	45mm	AESR45G	2.0mm	0.75mm	12mm
White	45mm	AESR45W	2.5mm	1.0mm	12mm
White	60mm	AESR60W	2.5mm	1.0mm	12mm
Orange	45mm	AESR45R	3.25mm	1.5mm	12mm
Orange	60mm	AESR60R	3.25mm	1.5mm	12mm
Purple	45mm	AESR45P	4.0mm	1.8mm	12mm
Purple	60mm	AESR60P	4.0mm	1.8mm	12mm
Black	60mm	AESR60B	5.0mm	2.2mm	15mm

Table 2. Approximate Equivalence for AEON™ Endostapler Reloads

AEON™ Endostapler			Endo GIA™ with Tri-Staple™ Technology		
Cartridge Color	Open Staple Height (mm)	Closed Staple Height (mm)	Cartridge Color	Open Staple Height (mm)	Closed Staple Height (mm)
Gray	2.0	0.75	Gray	2.0	0.75
White	2.5	1.0	Tan	2.0-3.0	0.75-1.25
Orange	3.25	1.5	Purple	3.0-4.0	1.25-1.75
Purple	4.0	1.8	Purple	3.0-4.0	1.25-1.75
Black	5.0	2.2	Black	4.0-5.0	1.75-2.25

STUDY DETAILS

Patients will be screened based on the inclusion and exclusion criteria below and will be consecutively evaluated for study enrollment. Each case will be randomly assigned to one of the two FDA approved endoscopic staplers. For the purposes of this study, the surgeons will either use the AEON™ Endostapler or the Endo GIA™ Reloads with Tri-Staple™ Technology and Ultra Universal Handle from Medtronic. Enrollment will be contingent on meeting these criteria, and the use of either the AEON™ Endostapler or the Endo GIA™ Reloads with Tri-Staple™ Technology from Medtronic. Study participation will begin once the subject signs the consent form and will end after the one-month postoperative follow up visit.

Selection of Subjects:

Inclusion Criteria

- Patients undergoing planned laparoscopic sleeve gastrectomy
- Informed consent for study obtained and signed from each subject

Exclusion Criteria

- Planned open surgical approach
- Use of staple line reinforcement material (buttress)
- Revision or other bariatric procedure
- Patients with a bleeding disorder: known coagulopathy, or Platelets <100,000, or PTT > 45sec, or PT> 15sec, or INR>1.5
- Patients with active HIV or Hepatitis B
- Patients under the age of 18 on the date of the surgery
- Patients who are pregnant
- Patients using tobacco products within the last 2 weeks prior to surgery date
- Patients using cortisone or related products within the last 2 weeks prior to surgery date

Withdrawal of Subjects:

Subjects are free to withdraw from the study at any time for any reason. Every effort will be made to determine why any subject withdraws from the study prematurely and this information will be recorded in the Clinical Study Report.

In addition, subjects may be withdrawn from the study by the Principal Investigator in consultation with the Sponsor for the following reasons:

- Adverse event
- Protocol violation
- Loss to follow-up

If a subject withdraws prematurely, all data normally collected by study completion should be collected at the time of premature discontinuation or at the scheduled discharge. All subjects who withdraw from

the study with an ongoing adverse event must be followed until the event is resolved or deemed stable. At the discretion of the PI, additional follow up visits may be done for subject safety.

Withdrawn subjects will be replaced, until 60 subjects complete the study.

Primary Outcome Measure:

- Incidence of intraoperative staple line bleeding from endoscopic or laparoscopic images as measured by the provided bleeding severity scale

Secondary Outcome Measures:

- Incidence of postoperative leakage requiring intervention through 30-day post-operative evaluation period
- Incidence of intraoperative or postoperative blood transfusion within 72 hours of surgery start time
- Hemoglobin difference between preop hemoglobin and hemoglobin on postoperative day #1 as well as difference between hemoglobin at recovery room and postoperative day #1
- Incidence of reported device-related adverse events through 30-day post-operative evaluation period
- Incidence of product malfunction during stapling
- Total hospitalization time
- Postoperative pain level per standard protocol (0-10 VAS scale completed at Recovery room, 6hrs postop and 7am at POD#1)
- Postoperative nausea presence (0-10 scale VAS completed at Recovery room, 6hrs postop and 7am at POD#1)
- Incidence of vomiting: incidence (at least one per patient) per stapler group, total episodes per group and emesis material (bloody or non-bloody)
- Correlation of number of reloads used and specimen lengths and maximum widths as measured by pathology examination
- Correlation of reload color used with observed bleeding and patient's stomach thickness by path exam
- Correlation of outcome parameters with BMI, visceral fat, gender and age
- Need for clipping the staple line prior to completion of the staple line

Steps and Procedures:

The study will include 60 total consecutive cases, randomized for stapler type: 30 with the AEON™ Endostapler and 30 with Endo GIA™ Reloads with Tri-Staple™ Technology. Surgeries will be performed by Dr. Yannis Raftopoulos.

All patients will undergo the standard preoperative evaluation pathway. Patients must sign informed consent for the operation.

All firings with the AEON™ Endostapler will be done with THICK MODE for the purposes of this study and shall conform to the AEON™ Instructions for Use. All firings with the Endo GIA™ Reloads with Tri-Staple™ Technology and Ultra Universal Handle should be done according to the Endo GIA™ Instructions for Use.

To measure incidence and degree of staple line bleeding, a third-party blinded evaluator will be used. No sutures, cautery or clips shall be applied during stapling for staple line bleeding, unless required at surgeon's discretion. Following the last firing, a member of the surgical or nursing team or the research coordinator present for the case will count 10 seconds and then capture images with the laparoscope. If bleeding from the staple line requires control prior to the last firing, an additional image should be captured before applying sutures, cautery, clips, etc. Five pictures will be obtained from each case: the pylorus, distal sleeve near the distal end of the staple line, mid-sleeve at the incisura angularis, proximal sleeve and GEJ near the proximal end of the staple line. These photographs will be sent by the research coordinator to the third-party evaluator either electronically or by mail. The third-party evaluator will be blinded to the device of each case. Upon receipt of photographs, the evaluator will evaluate staple line bleeding according to a provided Bleeding Severity Scale for Laparoscope Images (Appendix A) and record results in the Bleeding Severity Evaluation Sheet (Appendix E).

At the end of each case, the surgical team will fill out the relevant sections of the Data Collection Sheet (Appendix C).

Gastroscopy will be performed, per standard protocol, at the beginning of the case to suction all gastric contents and decompress the stomach as well at the completion of the sleeve gastrectomy. Evaluation for intraluminal bleeding will be performed at the last gastroscopy according to Appendix E. During the last gastroscopy, no suctioning of the gastric contents will be performed until evaluation for bleeding is made and pictures are obtained. The gastroscopy will be performed before any use of clipping at the staple line unless for circumstances judged by the surgeon to be medically necessary to do so before the endoscopy. These instances will also be recorded. Five pictures will be obtained from each case: the pylorus, distal sleeve near the distal end of the staple line, mid-sleeve at the incisura angularis, proximal sleeve and GEJ near the proximal end of the staple line. These photographs will also be sent to the third-party evaluator for evaluation of staple line bleeding according to a provided Bleeding Severity Scale for Endoscope Images (Appendix B). Results will be recorded in the Bleeding Severity Evaluation Sheet (Appendix E).

The determination of laparoscopic and endoscopic staple line bleeding will be based on the picture with the highest bleeding severity score for laparoscopic and endoscopic evaluation separately. Every effort will be made that all pictures prior to any suctioning of the staple line laparoscopically or endoscopically.

All typical post-operative care will continue, including immediate post-operative care prior to hospital discharge as well as the standard post-operative evaluation. A hemoglobin level will be checked at the

recovery room and at 5am on postoperative day #1 per standard protocol. This hemoglobin must be drawn from the upper extremity opposite from the one with the IV running fluids or at the same extremity with the IV running fluids but distal to the IV. For each post-operative period, a member of the surgical or nursing team will fill out the relevant sections of the Data Collection Sheet (Appendix C).

There will be no follow up study data collected after this point, however the patients will continue the standard follow up regimen per the physician's practice.

Surgery Locations:

Surgeries will take place at Holyoke Medical Center (575 Beech St, Holyoke, MA 01040).

Termination of the Study:

The Principal Investigator reserves the right to terminate the study in the interest of subject welfare. The Sponsor may terminate the study for administrative reasons.

Should the study be terminated, all documentation pertaining to the study must be returned to the Sponsor. Any actions required to assess or maintain study subject safety will continue as required, despite termination of the study by the Sponsor.

Protocol Deviations:

Deviations from the protocol will be assessed as "minor" or "major" in agreement with the Sponsor. Major deviations from the protocol may lead to the exclusion of a subject from data analysis and will be considered on a case-by-case basis.

The Investigator will not deviate from this protocol for any reason without prior written approval from the Sponsor, except in cases of medical emergencies. The Investigator may deviate from the protocol without prior approval only when the change is necessary to eliminate an apparent immediate hazard to a subject. In that event, the Investigator will notify the Sponsor immediately by phone, notify the IRB, and confirm notification to the Sponsor in writing within 5 working days after the change is implemented.

Risks:

There are no additional risks to the patients participating in the study other than the known risks of the chosen procedure the sleeve gastrectomy. These known risks will be explained to the participating patients through the standard consent used for this procedure. In addition, there are no known additional risks from the use of either stapler. Both staplers are FDA approved and the surgeon-investigator of this study as well as the OR staff is very familiar with both staplers and loads. The surgeon has used both staplers and loads extensively in the past (>20 bariatric cases) and he is past the learning curve for either one.

Statistics:

This is an open-label study (since the patient will be blinded and the evaluation for the primary outcome will be done by a third party blinded to the stapler used). Formal sample size calculations were not performed as the purpose of the study is to demonstrate non-inferiority. The number of subjects was chosen based on feasibility and is considered sufficient to meet the study objectives.

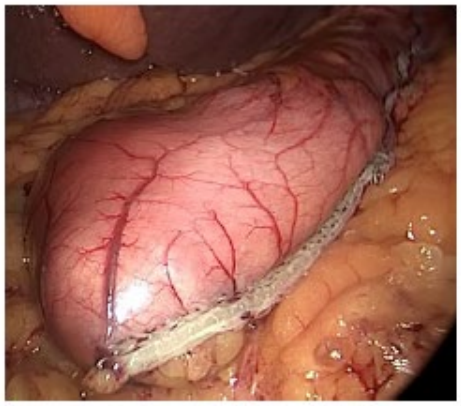
Detailed methodology for summary and statistical analyses of the data collected in this study will be documented in the Clinical Study Report. T-test and chi-square test will be used for univariate analysis of continuous and categorical data respectively. Regression analysis may be used to identify the independent effect of several parameters on primary or secondary outcomes if there are statistically significant differences in univariate analysis.

Direct Access to Source Data/Documents:

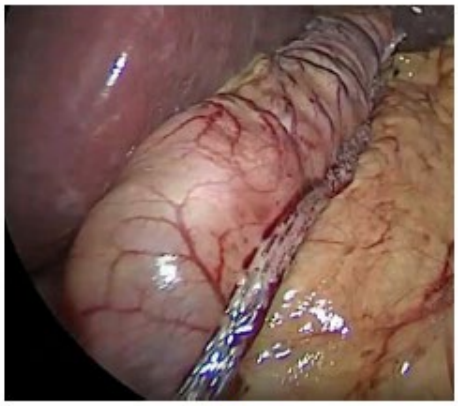
The Principal Investigator will ensure that the Sponsor, IRB, and regulatory authorities will have direct access to all study sites, source data/documents, and reports for the purpose of monitoring and auditing. In the event that other study-related monitoring should be done by other parties, those parties will be required to sign a confidentiality agreement prior to any monitoring or auditing.

Appendix A – Bleeding Severity Scale for Laparoscope Images

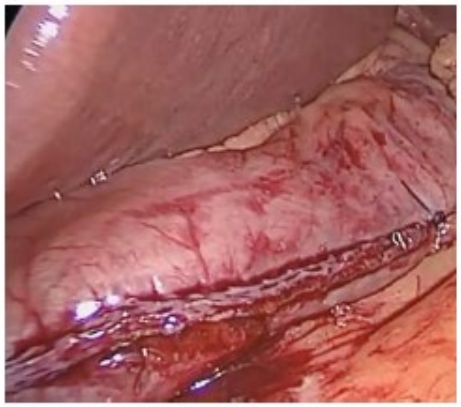
Bleeding Severity Scale



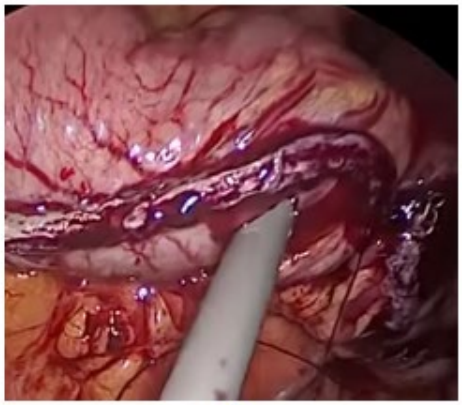
1



2



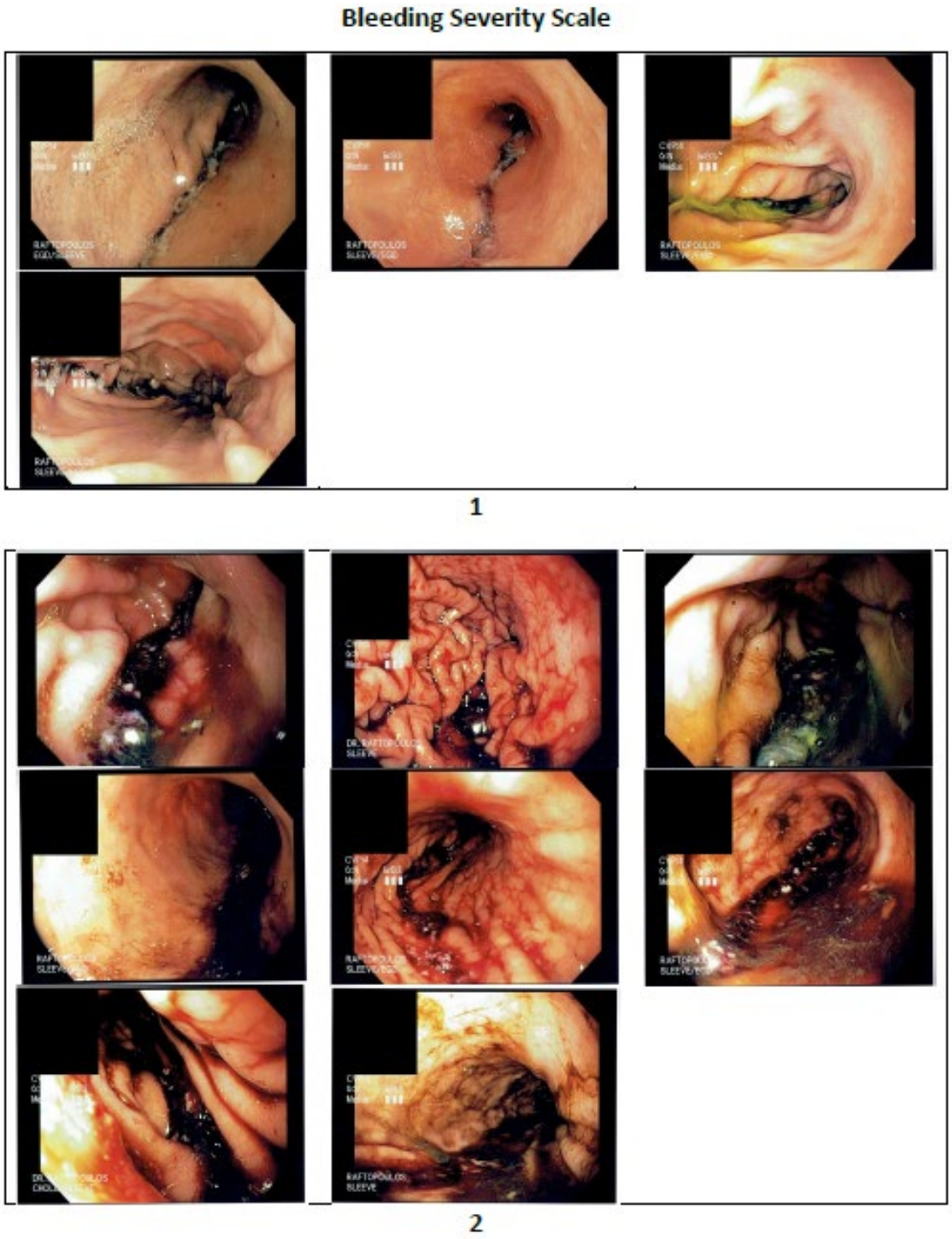
3



4

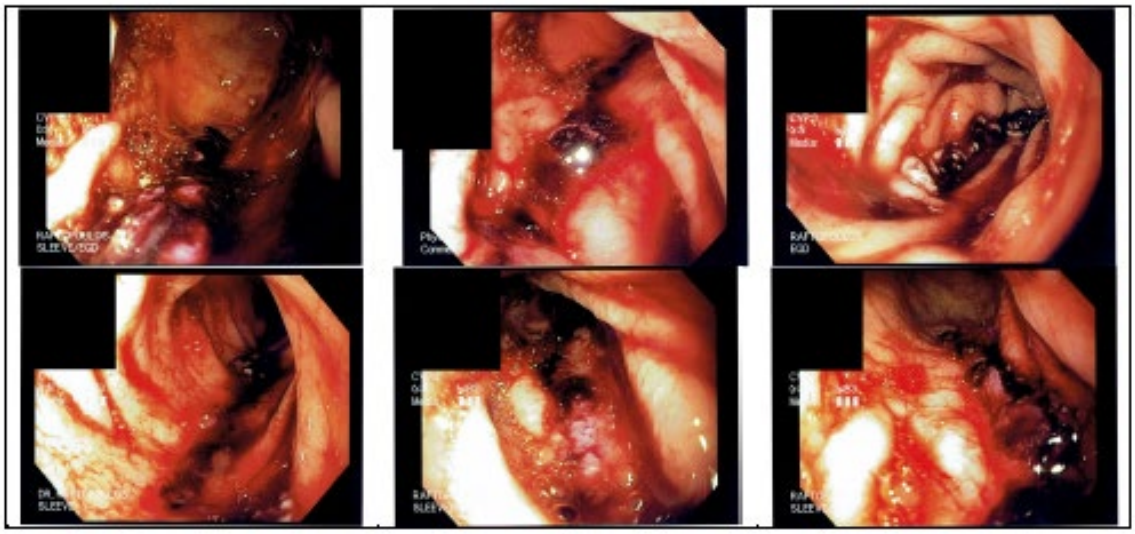
5

Appendix B – Bleeding Severity Scale for Endoscope Images

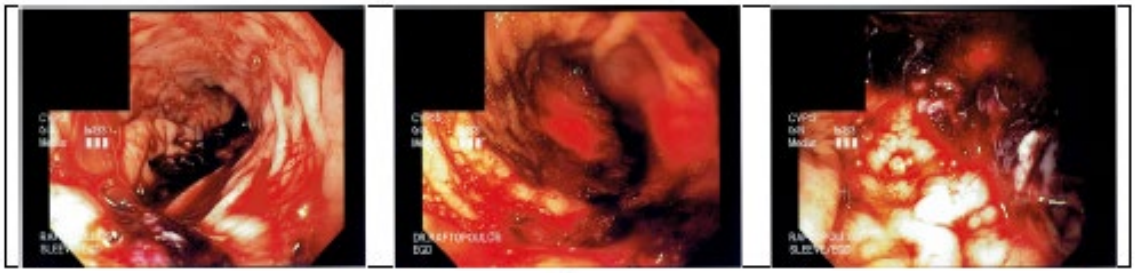


Appendix B – Bleeding Severity Scale for Endoscope Images (continued)

Bleeding Severity Scale



3



4

5

Appendix C – Data Collection Sheet

Surgery Date: _____ Surgeon: _____ Hospital: _____

Stapler Type (Circle): AEON™ Endostapler Endo GIA™ with Tri-Staple™ Technology

Patient Gender: _____ Patient Age: _____ Patient BMI: _____

AEON™ Endostapler	Black 60mm	Purple 60mm	Purple 45mm	Orange 60mm	Orange 45mm	White 60mm	White 45mm
Quantity Reloads Used							

Endo GIA™ with Tri-Staple™ Technology	Black 60mm	Black 45mm	Purple 60mm	Purple 45mm	Tan 60mm	Tan 45mm
Quantity Reloads Used						

Intraoperative Outcomes		
Product malfunction during stapling? (circle one)	Yes	No
Blood transfusion due to staple line bleeding? (circle one)	Yes	No
Visceral fat:		
Clips required for bleeding (non-routine)? (circle one)	Yes	No

If yes to any above, please specify:

Postoperative Outcomes				
	Pre-op	**Recovery**	**6 Hours**	**POD #1**
Pain level per standard protocol (0-10 VAS scale):	N/A			
Nausea level per standard protocol (0-10 VAS scale):	N/A			
Hemoglobin:			N/A	
72 Hours				
Blood transfusion due to staple line bleeding? (circle one)	Yes		No	
30 Days				
Total hospitalization time:				
Number of vomiting episodes:		Bloody	Non-bloody	
Reported device-related adverse events? (circle one)	Yes		No	
Postoperative leakage requiring intervention? (circle one)	Yes		No	

If yes to any above, please specify:

Appendix D – Pathology Exam Data Sheet

Exam Date: _____ Case #: _____

Specimen Length:	
Maximum Width:	
Stomach Thickness:	

Appendix E – Bleeding Severity Evaluation Sheet

Evaluation Date: _____ Evaluator: _____

Case #	Staple Line Image from Laparoscope	Staple line bleeding per Bleeding Severity Scale (choose one):				
		No bleeding	Minimal bleeding	Moderate bleeding	Excessive bleeding	Profuse bleeding
	A. Pylorus	1	2	3	4	5
	B. Distal sleeve near distal end	1	2	3	4	5
	C. Distal sleeve	1	2	3	4	5
	D. Proximal sleeve	1	2	3	4	5
	E. GEJ near proximal end	1	2	3	4	5

Case #	Staple Line Image from Endoscope	Staple line bleeding per Bleeding Severity Scale (choose one):				
		No bleeding	Minimal bleeding	Moderate bleeding	Excessive bleeding	Profuse bleeding
	F. Pylorus	1	2	3	4	5
	G. Distal sleeve near distal end	1	2	3	4	5
	H. Distal sleeve	1	2	3	4	5
	I. Proximal sleeve	1	2	3	4	5
	J. GEJ near proximal end	1	2	3	4	5