Statistical Analysis Plan (SAP)

A Prospective, Randomized, Controlled, Multi-Center Evaluation of a Powered Vascular Stapler in Video-Assisted Thoracoscopic Lobectomies

Protocol Number: ESC-15-001

Protocol Version: Original, November 11, 2015

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The following individuals have reviewed this version of the Statistical Analysis Plan and are in agreement with the content:

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Revision History

Revision Number	Revision Date	Reasons for Revision
1.0	27MAR2017	Original Document

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This is the Statistical Analysis Plan (SAP) for the final analysis of data collected under Protocol ESC-15-001. This SAP describes in detail the statistical methodology and statistical analyses for the above mentioned protocol.

1 Study Overview

1.1 **Study Objectives**

The primary objective of the study is to demonstrate that the frequency of hemostatic interventions/procedures required intra-operatively or post-operatively related to the transection of the pulmonary artery (PA) and pulmonary vein (PV) during VATS lobectomy with the ECHELON FLEX™ Powered Vascular Stapler (PVS) is not increased when compared to standard of care (SOC) during video-assisted thoracoscopic surgery (VATS) lobectomy.

1.2 **Study Design**

This is a prospective, randomized, controlled, multi-center, open-label study that will collect and compare data from the surgeon's current SOC stapler (for PA/PV transection) and PVS. Prospective subjects will be informed about the nature of the research, given the informed consent document (ICD) to read, and if the subject understands the consent, will be asked to provide written consent.

2 Treatment Assignment

Subjects were assigned to either the surgeon's current SOC stapler or PVS. The ECHELON FLEX™ PVS with Advanced Placement Tip is a sterile, single use instrument that simultaneously cuts and staples tissue. There are four staggered rows of staples, two on either side of the cut line. The ECHELON FLEX™ PVS with Advanced Placement Tip and reloads have a staple line that is approximately 35mm long and a cut line that is approximately 30 mm long. The shaft can rotate freely in both directions and an articulation mechanism enables the distal portion of the shaft to pivot to facilitate lateral access to the operative site. The powered vascular stapler has been cleared for marketing by the FDA and is CE marked which allows for commercial distribution in the European Union. The device will be used in accordance with its product labeling and Instructions for Use.

3 Randomization and Blinding Procedures

Subjects were randomized to either the surgeon's current SOC stapler or PVS in a 1:1 ratio. Randomization could occur at any time prior to surgery up to transection of the vessel(s). Sites were instructed to wait until as close as possible to the actual time of vessel transection so as to minimize randomized drops within the study.

Randomization was accomplished through utilization of envelopes at the study site. Randomization envelopes were created according to the "Work Instructions for the Creation of Randomization Envelopes", document number WE001625, based on a randomization schedule generated by the Ethicon Biostatistics group. The randomization schedule was generated using a validated program that incorporated variable block sizes and treatment assignment was balanced within each study site. This was an open-label study and therefore no blinding procedures were required.

4 Interval Windows

Interval windows are not defined for the purpose of analysis in this study as the collection of data for the primary performance endpoint occurs intra-operatively and the collection of data for the primary safety endpoint occurs through hospital discharge. The final visit occurred approximately 4 weeks after surgery, thus no interval windows need to be defined given the absence of long-term follow-up in this study. The complete Schedule of Events for this study can be found in the Synopsis of the study protocol.

5 Primary and Secondary Endpoints

5.1 Primary Performance Endpoint

The primary performance (effectiveness) endpoint in this study was defined as the occurrence of hemostatic interventions/procedures completed for intra-operative bleeding related to the transection of the PA and PV during VATS lobectomy with the use of either the SOC or PVS stapler. Hemostasis interventions or procedures were defined as bleeding detected and controlled intra-operatively (additional stapling, over-sewing, clip placement, compression, use of suture, sealant, and/or buttress, and/or use of energy); or bleeding that occurred intra-operatively requiring blood or blood product transfusion or an additional surgical procedure (e.g. conversion to open). No hemostasis intervention was defined as no bleeding at the staple line or bleeding that stopped after initial blotting of the staple line.

The primary performance endpoint will be summarized at the firing level as multiple firings per subject were expected and observed; that is, the denominator for the primary endpoint will be the total number of firings and the numerator will be the number of firings where an intervention was required.

During development of the protocol with the Notified Body (TUV) following their decision to grant CE mark to the device, a formal hypothesis was not defined for the study; however, to establish that the intervention rate of PVS is not increased compared to SOC, an acceptance criterion was developed and a 95% confidence interval for the difference in proportion of firings requiring interventions for PVS minus SOC will be calculated. The powered vascular stapler will be considered to have acceptable performance if the upper bound of the 95% confidence interval does not exceed 3%.

5.2 Primary Safety Endpoint

The primary safety endpoint was defined as the occurrence of hemostatic interventions/procedures completed for post-operative bleeding related to the transection of the PA and PV during VATS lobectomy with the use of SOC or PVS. Hemostasis intervention was defined as bleeding that occurred post-operatively requiring blood or blood product transfusion or an additional surgical procedure (related to PA and PV transection). No hemostasis intervention was defined as no interventions needed for post-operative bleeding (related to PA and PV transection). This endpoint was recorded at the subject level as it was based on post-operative interventions and not specific to any individual firing.

5.3 Secondary and Additional Endpoints

Key additional endpoints in this study include: pain score assessments, American Shoulder and Elbow Surgeons Standardized (ASES) Shoulder Assessment, Surgeon Task Load Index, adverse events, and device usability questionnaires.

6 Levels of Significance

Evaluation of the acceptance criterion for this study is being accomplished through estimation of a 95% confidence interval. No hypotheses are specified for this study and no p-values are being calculated, therefore no level of significance is specified. All estimation of additional endpoints will be performed using 95% confidence intervals.

7 Analysis Sets

There will be three analysis sets defined:

- The Full Analysis Set (FAS) will consist of all randomized subjects who had a procedure performed and provide data on the number of surgical interventions;
- The Per Protocol (PP) Analysis Set will consist of all subjects in the FAS who had no major protocol violations;
- The Safety Analysis Set consists of all randomized subjects on whom a procedure is started.

The primary performance endpoint analysis will be performed on the Full Analysis Set and subjects will be classified according to their randomized treatment group. The primary performance endpoint analysis will also be performed on the PP set as a sensitivity analysis to the results on the FAS. The summary of additional endpoints will also be performed on the Full Analysis Set. Analysis of the primary safety endpoint and adverse events summaries will be performed on the Safety Analysis Set.

8 Sample Size Justification

Approximately 200 subjects were randomized in the study in a 1:1 ratio to SOC or PVS. Historical clinical study data on a similar powered surgical stapler demonstrated a need for staple line

interventions in approximately 6% of firings on the pulmonary artery or pulmonary vein. This data also showed an average of 2.6 to 2.9 firings per subject, and it was expected, given differences in device design, that each subject would require 3 to 4 firings on the pulmonary vein or pulmonary artery in the current study with PVS.

Given that it is expected to have a minimum of 260 firings in each group, the sample size of approximately 200 subjects is considered adequate for descriptive summarization of the primary performance endpoint, i.e. number and frequency of intra-operative surgical interventions. Assuming an approximate background intervention rate of 6% in each group, the given sample size will provide reasonable precision in the estimation of the intervention rate in each treatment group to an expected margin of error for a 95% confidence interval of at most 2.9%.

9 Data Monitoring Committee (DMC)

No Data Monitoring Committee was planned or utilized during this study.

10 Analyses to be Conducted

10.1 General Conventions

Subject data will be summarized using listings and tables. All eCRF data will be listed per subject for all subjects. Descriptive statistical analyses will be provided for pre-specified study endpoints. Summaries for continuous variables will include number of observations (n), mean, standard deviation, median, minimum, and maximum. Summaries for categorical variables will include number and percentage.

Analyses will be conducted using SAS software version 9.4 or higher. During the course of analysis programming of tables that are mocked up in this SAP, minor modifications may become necessary. Examples of these minor modifications include, but are not limited to, re-wording of a footnote, addition of a footnote, re-labeling of a column, or addition or removal of a column from a listing. In cases where modifications to tables or listings are not related to a change in statistical analysis methodology or conclusions that could be made on the originally proposed methodology, then no amendment of the SAP is necessary. Amendment of the SAP is required in any case where changes to statistical analyses that were planned in the original signed SAP are proposed.

10.2 Disposition of Study Subjects

Subject disposition will be summarized by randomized treatment group and overall using counts and percentages. The number and percentage of subjects in each analysis set will be tabulated. Additionally, the number and percentage of subjects completed and discontinued will be tabulated along with the specific reasons for discontinuation.

10.3 Demographic, Baseline, and Surgical Characteristics

Summary statistics of subject demographics (age, gender, race, and ethnicity) will be presented by randomized treatment group and overall for the Full Analysis Set. Surgical characteristics including, at minimum, lobe location, calcified hilar lymph node presence, number of ports used, number of pulmonary arteries transected, number of chest tubes placed, ASA physical status, estimated blood loss, conversion to open, requirement for blood transfusion, procedure duration, and number of chest tubes will be summarized by randomized treatment group and overall. Results of tumor assessments performed by the pathology laboratory (including tumor stage, maximum tumor diameter, maximum tumor depth, primary TNM classification, presence of distant metastasis, and confirmation of non-small cell lung cancer) will also be summarized by randomized treatment group and overall.

10.4 Primary Endpoint Analyses

For the primary performance endpoint, summary statistics and 95% confidence intervals will be provided for the number and frequency of interventions for the set of SOC subjects and PVS subjects separately. This will be performed based on the total number of firings. An intervention is defined as any firing which is classified as a hemostasis intervention. To establish that the intervention rate is not increased compared to SOC, a 95% confidence interval for the difference in the proportion of firings requiring interventions for PVS minus SOC will be calculated and the powered vascular stapler will be considered to have acceptable performance if the upper bound of the 95% confidence interval does not exceed 3%.

The following SAS code will be used to generate 95% confidence intervals for the individual treatment groups as well as the difference between groups:

```
proc sort data=hemo_interv;
  by TrtGroup descending event;
run;
proc freq data=hemo_interv order=data;
  tables TrtGroup*event/binomial riskdiff;
run;
```

This code assumes that the dataset hemo_interv contains one record per firing, the variable ‘TrtGroup’ contains the identifier for randomized treatment group (the SOC group should be listed in the first row of the table), and the variable ‘event’ identifies an occurrence of the primary endpoint with a 1 and no occurrence of the primary endpoint with a 0. The resulting output in the Column 1 Risk Estimates table in the SAS Output Window provides the individual confidence intervals for each treatment group as well as the confidence interval for the difference between groups.

Additional summaries will be provided to tabulate the total number of vessels transected as well as the specific type of vessel that was transected – pulmonary artery or pulmonary vein. The specific types of interventions that were performed will also be tabulated by randomized treatment group.

The same analysis will be replicated for the primary safety endpoint for the occurrence of hemostatic interventions/procedures completed for post-operative bleeding related to the transection of the PA and PV during VATS lobectomy at the subject level. A similar dataset will be created that contains one record per subject and an indicator for whether or not the subject experienced a post-operative intervention event.

10.5 Plans for Interim Analysis

No interim analyses were planned or performed for this study.

10.6 Handling of Missing Data

All summaries will be performed only on subjects undergoing the surgical procedure and only observed data will be summarized. There will be no imputation of data for early terminated subjects or for missing data within the database.

10.7 Sensitivity Analyses

Analyses of the primary performance and safety endpoints will be replicated on the Per Protocol Set to assess the primary results in the set of subjects with no major protocol violations.

10.8 Subgroup Analysis

No subgroup analyses are planned for this study.

10.9 Assessment of Site Homogeneity

No summaries or adjustments by study site are planned for this study.

10.10 Additional Endpoint Analyses

Device usage details will be summarized with counts and percentages for subjects in whom the device was articulated during the surgical procedure. Summaries will be provided by randomized treatment group and in total. Similar summaries will also be provided for the surgeon satisfaction questionnaire and the surgeon device questionnaire (administered only in PVS cases).

Post-operative pain is assessed at Visit 3 and Visit 4. Subjects are asked to rate their pain on a scale ranging from 0 (no pain) to 10 (worst possible pain). Subjects will rate pain relating to three sites – trocar site, incisional site, and chest tube site. Summary statistics will be provided at Visits 3 and 4, as well as the change from Visit 3 to Visit 4. No inferential comparisons between treatment groups are planned.

Summary statistics will be provided for the Surgery Task Load Index (Surg-TLX). Surgeons are asked to rate 6 specific components after each surgery performed. The 6 components are – mental fatigue, physical fatigue, hurried/rushed pace, procedure complexity, anxious while performing procedure, and distracting operating environment. Each component is scored on a 0 to 100 scale with lower scores representing a 'Low' response on that component and higher scores indicating a 'High' response on that component. Summaries will also be provided for an overall score which is calculated as the average of the six components for each surgery.

The ASES Shoulder Assessment is a patient reported outcome designed to measure functional limitations and pain of the shoulder and has been adapted to this study to measure upper body functionality following VATS lobectomy. The assessment utilizes 10 questions that are answered with: unable to do = 0, very difficult to do = 1, somewhat difficult to do = 2, and not difficult = 3. Scores for each subject are obtained by summing the responses to the 10 questions and thus range from 0 to 30. Summary statistics will be provided for the ASES Shoulder Assessment at Visit 1 (prior to surgery), Visit 3 (after surgery, prior to discharge), and Visit 4 (approximately 4 weeks after surgery). Summary statistics will also be provided for the change from Visit 1 to Visit 3, and for the change from Visit 1 to Visit 4.

The total number of protocol deviations will be tabulated by treatment group and in total. Specific types of protocol deviations will also be summarized with counts and percentages. The number and percentage of subjects with at least one protocol deviation will also be summarized.

10.11 Safety Analyses

Safety will be assessed through the incidence of adverse events (AEs) and serious adverse events (SAEs), which will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The number and percentage of subjects reporting AEs and SAEs will be summarized at the MedDRA system organ class and preferred term level by treatment group and overall. Similar summaries will also be provided for AEs and SAEs related to the study device, as well as for AEs and SAEs related to the study procedure. Related events are those where the relationship is indicated as Possibly, Related, or Unknown. The incidence of AEs will also be summarized by maximum severity. All reported adverse events will be listed.

Appendix: Table Shells and List of Listings to be Generated

Table shells are provided below for all summaries to be generated for this study. Additionally, a list of all listings to be created is provided corresponding to the eCRFs that were used during this study. All fields collected will be listed.

Table 1
Subject Disposition
All Subjects

	Standard of Care Stapler	Powered Vascular Stapler	Total
Signed Informed Consent			xx
Randomized	xx	xx	xx
Safety Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Full Analysis Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinued from the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation			
Withdrawal of consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Surgical	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Site or Study Termination	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: All percentages are based on the number of subjects in the Safety Set as the denominator.

Table 2
Subject Demographics
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Race			
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity			
Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Non-Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Age (years)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Gender			
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 3
Protocol Deviations
Safety Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total Number of Protocol Deviations	xxx	xxx	xxx
Specific Types of Protocol Deviations [1]			
Informed Consent Process	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Inclusion/Exclusion Criteria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Randomization	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study Procedure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Visit Out of Window	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sponsor Assessment of Protocol Deviations [1]			
Minor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Major	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number (%) of Subjects With at Least 1 Protocol Deviation [2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

1. Denominator used is the total number of protocol deviations reported.
2. Denominator used is the total number of subjects in the column header.

Table 4
Surgical Characteristics
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Location of Affected Lobe			
Left Lung, Superior Lobe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Left Lung, Inferior Lobe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Left Lung, Multiple Lobes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Right Lung, Superior Lobe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Right Lung, Middle Lobe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Right Lung, Inferior Lobes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Right Lung, Multiple Lobes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Calcified Hilar Lymph Nodes Present?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Pulmonary Arteries Transected			
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Ports			
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Chest Tubes Placed Intraoperatively			
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ASA Physical Status			
Class I	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Class II	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Class III	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 4
Surgical Characteristics
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Estimated Blood Loss (mL)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Transfusion of Blood or Blood Product Required?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Procedure Converted to Open?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Procedure Duration (min)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Chest Tube Duration (nights)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Programming Note: Chest tube duration is calculated from date of surgery to date of final chest tube removal

Table 5
Tumor Assessment – Pathology Lab
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Tumor Stage, Confirmed by Pathology			
Stage 0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIIA	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IIIB	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stage IV	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Maximum Tumor Diameter (cm)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Maximum Tumor Depth (cm)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Primary Tumor TNM Classification			
TX	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tix	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T1a	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T1b	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
T4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 5
Tumor Assessment – Pathology Lab
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
TNM Classification for Regional Lymph Node			
NX	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
N3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Distant Metastasis Present?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tumor Confirmed by Pathology as Non-Small Cell Lung Cancer?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 6
Intra-Operative Interventions on Pulmonary Artery or Pulmonary Vein
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total Number of Vessels Transected	xxx	xxx	xxx
Pulmonary Artery	xxx	xxx	xxx
Pulmonary Vein	xxx	xxx	xxx
Number of Vessel Transections Requiring Intervention [1]			
n (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
95% Confidence Interval for Percent	xx.x%, xx.x%	xx.x%, xx.x%	xx.x%, xx.x%
Difference (95% CI) for Percent Requiring Transection [2]	xx.x% (xx.x%, xx.x%)		
Type of Intervention, n (%) [3]			
Additional Stapling	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Over-sewing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Compression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Use of Suture	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sealant	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Buttress	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Use of Energy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Clip Placement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Product Transfusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Additional Surgical Procedure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other Intervention	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Denominator for calculation of percentage is the total number of vessels transected in that group.
[2] Difference is calculated as Powered Vascular Stapler minus Standard of Care Stapler.
[3] Denominator for calculation of percentage is the total number of vessels requiring intervention in that group.

Table 7
Post-Operative Interventions or Procedures Related to Pulmonary Artery or Pulmonary Vein Bleeding
Safety Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Number of Subjects Requiring Post-Operative Intervention Related to Pulmonary Artery or Pulmonary Vein Bleeding			
n (%) [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
95% Confidence Interval for Percent	xx.x%, xx.x%	xx.x%, xx.x%	xx.x%, xx.x%
Type of Intervention, n (%) [2]			
Blood Product Transfusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Additional Surgical Procedure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other Intervention	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Denominator for calculation of percentage is the total number of subjects in that group.
[2] Denominator for calculation of percentage is the total number of subjects requiring intervention in that group.

Table 8
Device Usage Details
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Number of Subjects Where Device Was Articulated	xxx	xxx	xxx
Did Articulation Make it Easier to Perform Surgery? [1]			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Was Articulation Essential to Performing the Surgery? [1]			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Was the Angle Range of the Device Sufficient? [1]			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

1. Denominator used is the total number of subjects in whom the device was articulated.

Table 9
Surgery Task Load Index (SURG-TLX)
Full Analysis Set

Characteristic	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Overall Score			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Mentally Fatiguing			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Physically Fatiguing			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
Standard Deviation	x.xxx	x.xxx	x.xxx
Median	xx.x	xx.x	xx.x
Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Similar summaries for remaining components:			
Hurried/Rushed Pace			
Procedure Complexity			
Anxious While Performing Procedure			
Distracting Operating Environment			

Note: Each component is scored on a 0 to 100 scale with lower scores representing a ‘Low’ response and higher scores representing a ‘High’ response.

Table 10
Surgeon Satisfaction Questionnaire
Full Analysis Set

Characteristics	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
How Satisfied Were You With Device Usability?			
Very Unsatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unsatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Amount of Tissue Slippage			
No Tissue Slippage	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Some Tissue Slippage	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Extensive Tissue Slippage	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 11
Post-Operative Pain Score
Full Analysis Set

Pain Component	Time Point Statistic	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Trocar Pain	Visit 3			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Visit 4			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Change From Visit 3 to Visit 4			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Same summary will be repeated for:
Incisional Pain
Chest Tube Pain

Programming note: Change from Visit 3 to Visit 4 will be calculated as Visit 4 value minus Visit 3 value.

Note: For each pain component, the subject is asked to rate his or her pain today on a scale from 0 (no pain) to 10 (worst possible pain).

Table 12
Surgeon Device Questionnaire
Full Analysis Set

Question Response	Powered Vascular Stapler (N = ##)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip enables easier placement of the device on vessels compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip has the potential to reduce the amount of dissection required (otomy) around the vessel to place the stapler compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip has the potential to reduce the surgeon stress during the most challenging step of the procedure, which is the pulmonary artery / pulmonary vein transection, compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)
The ECHELON FLEX Powered Vascular Stapler with Advanced Placement Tip allows for the precise control and placement of the end effector on the target vessel compared to your current standard of care device:	
Strongly Disagree	xx (xx.x%)
Slightly Disagree	xx (xx.x%)
Neutral	xx (xx.x%)
Agree	xx (xx.x%)
Strongly Agree	xx (xx.x%)

Table 13
ASES Shoulder Assessment
Full Analysis Set

Shoulder Side	Time Point Statistic	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Right	Visit 1			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Visit 3			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Change From Visit 1 to Visit 3			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Visit 4			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
	Change From Visit 1 to Visit 4			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	Standard Deviation	x.xxx	x.xxx	x.xxx
	Median	xx.x	xx.x	xx.x
	Minimum, Maximum	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Same summary will be repeated for: Left Side

Programming note: Change from Visit 1 to Visit 3 will be calculated as Visit 3 value minus Visit 1 value.

Table 14
Adverse Events by System Organ Class and Preferred Term
Safety Set

System Organ Class	Preferred Term	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 2		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 3		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 4		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The following tables will have the same format as Table 14:

Table 15	Serious Adverse Events by System Organ Class and Preferred Term Safety Set
Table 16	Adverse Events Related to the Study Device by System Organ Class and Preferred Term Safety Set
Table 17	Serious Adverse Events Related to the Study Device by System Organ Class and Preferred Term Safety Set
Table 18	Adverse Events Related to the Study Procedure by System Organ Class and Preferred Term Safety Set
Table 19	Serious Adverse Events Related to the Study Procedure by System Organ Class and Preferred Term Safety Set

Table 20
Adverse Events by System Organ Class, Preferred Term and Maximum Severity
Safety Set

System Organ Class	Preferred Term	Standard of Care Stapler (N = ##)	Powered Vascular Stapler (N = ##)	Overall (N = ##)
Total		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 2		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The following listings will be generated for this study:

Listing 1	Inclusion/Exclusion Criteria All Subjects
Listing 2	Demographics All Subjects
Listing 3	Medical History All Subjects
Listing 4	Surgical History All Subjects
Listing 5	Inclusion/Exclusion at Surgery and ASA Status All Subjects
Listing 6	Procedure Details All Subjects
Listing 7	Procedure Time Duration All Subjects
Listing 8	Intra-Operative Interventions on Pulmonary Artery and Pulmonary Vein All Subjects
Listing 9	Bronchus and Parenchyma Transections All Subjects
Listing 10	Intra-Operative Interventions Not on Pulmonary Artery and Pulmonary Vein All Subjects
Listing 11	Device Usage Details All Subjects
Listing 12	Tumor Assessment Log All Subjects
Listing 13	Surgeon Device Questionnaire (PVS Only) All Subjects
Listing 14	Surgery Task Load Index All Subjects
Listing 15	Surgeon Satisfaction Questionnaire All Subjects

Listing 16	Post-Operative Interventions on Pulmonary Artery and Pulmonary Vein All Subjects
Listing 17	Pain Score Assessment All Subjects
Listing 18	Chest Tube Details Log All Subjects
Listing 19	Adverse Events All Subjects
Listing 20	Concomitant Medications All Subjects
Listing 21	Concomitant Procedures/Interventions All Subjects
Listing 22	Protocol Deviations All Subjects
Listing 23	Completion/Withdrawal All Subjects
Listing 24	Study Visits All Subjects